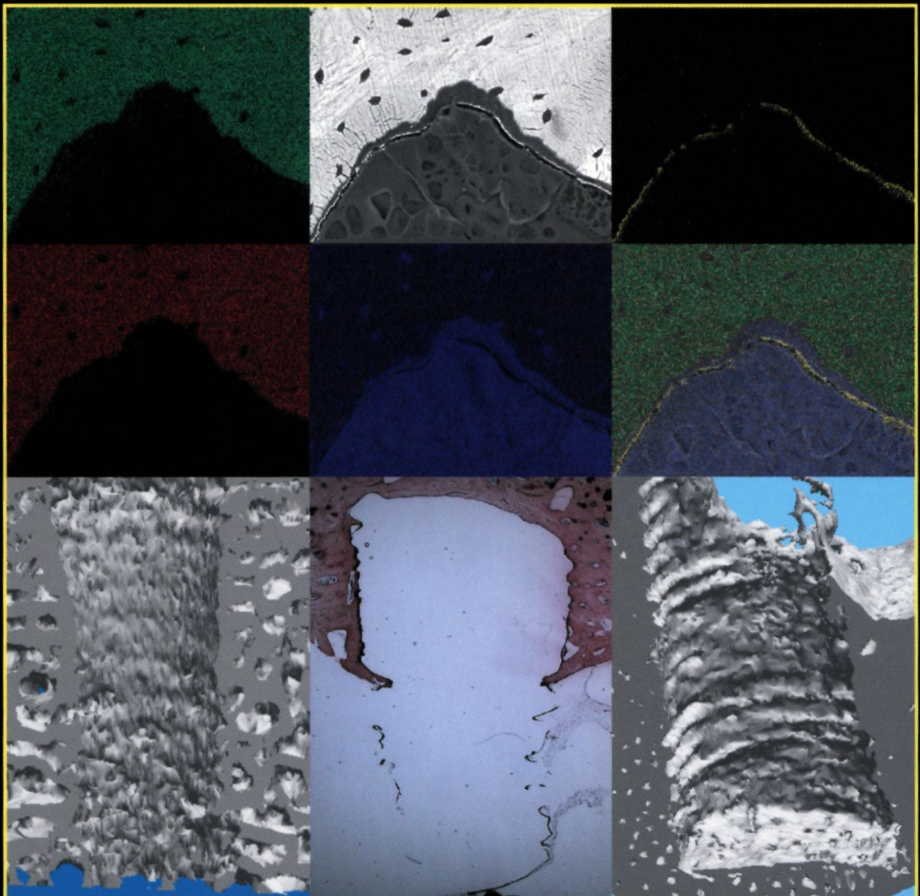
Oral Implants:
Effects of Surgical Technique on Implant Fixation



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Oral Implants: Effects of Surgical Technique on Implant Fixation /
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Thesis Radboud University Nijmegen Medical Centre.

Oral Implants:
Effects of Surgical Technique on Implant Fixation

een wetenschappelijke proeve op het gebied van de Medische Wetenschappen

Proefschrift

ter verkrijging van de graad van doctor
aan de Radboud Universiteit Nijmegen
op gezag van de Rector Magnificus prof. dr. C.W.P.M. Blom,
volgens besluit van het College van Decanen
in het openbaar te verdedigen op maandag 18 december 2006
des namiddags om 1:30 uur precies
door

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geboren op 18 mei 1968
te Riyadh (Saoedie Arabie)

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Oral Implants:
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A scientific essay in Medical Sciences

Doctoral thesis

to obtain the degree of doctor
from the Radboud University of Nijmegen,
on the authority of the Rector Prof dr C W P M Blom,
according to the decision of the Council of Deans
to be defended in public on Monday 18th December, 2006
at 1 30 pm precisely
by

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Dedicated to:
My parents
My
husband
My children

This thesis is based on the following publications

- Implant surface roughness and bone healing A systematic review Shalabi MM, Gortemaker JG, Van't Hof MA, Jansen JA, Creugers NHJ *Journal of Dental Research* 85 496-500 (2006)
- The effects of implant surface roughness and surgical technique on implant fixation in an *in vitro* model Shalabi MM, Wolke JGC, Jansen JA *Journal of Clinical Oral Implants Research* 17 172-178 (2006)
- A meta-analysis of clinical studies to estimate the 4 5 year survival rate of implants inserted with the osteotome technique Shalabi MM, Manders P, Mulder J, Jansen JA, Creugers NHJ *International Journal of Oral & Maxillofacial Implants* (accepted)
- A mechanical evaluation of implants placed with different surgical techniques into the trabecular bone of goats Shalabi MM, Johannes G C Wolke JGC, de Ruijter AJE, Jansen JA *Journal of Oral Implantology* (accepted)
- A histological evaluation of oral implants inserted with different surgical technique into the trabecular bone of goats Shalabi MM, Wolke JGC, de Ruijter AJE, Jansen JA *Journal of Clinical Oral Implants Research* (accepted)
- Bone response to titanium coated polymethyl methacrylate resin (PMMA) implants inserted into the tibia of goats Shalabi MM, Wolke JGC, Cuijpers VM , Jansen JA *Journal of Materials Science Materials in Medicine Clinical Oral Implants Research* (submitted)

Contents

Chapter 1

General introduction

1. Introduction

In the early 1960s, Branmark and co-workers started developing a novel oral implant that for clinical function depended on direct bone anchorage – termed osseointegration Later, Albrektsson *et al* (1981) presented information on a series of background parameters that needed control in order to ensure the occurrence of a reliable osseointegration of an implant These parameters involve (1) the biocompatibility, (2) design and (3) surface conditions of the implant, (4) the status of the host bed, (5) the surgical technique at insertion, and (6) the loading applied afterwards

Further, it has to be noticed that the damage to the soft and hard tissue during implant installation initiates the process of wound healing, which eventually allows the implant to become Osseo- integrated and the establishment of a delicate mucosal barrier to the implant

Besides implant surface characteristics, improvements of the surgical technique seem to be a reliable way of increasing oral implant success It may be premature to regard surface-modified implants as out-of-date, but the fact remains that the only available controlled clinical studies (*i e*, Pchades-Roman 2000, Gotfredsen & Karlsson 2001, Engquist 2002) comparing smooth turned and roughened implants have failed to demonstrate any clear preference for the roughened implants (Albrektsson 2001)

Although, there are a great number of scientific investigations about Osseo-integrated implants, more basic science is needed to learn more about optimal biomaterials, designs and surfaces of oral implants in relation to the applied surgical technique for implant installation

Along these lines, this chapter will focus on the relevance of implant surface topography of endosseous oral implants as well as surgical considerations and technique of implantation

2. Surface topography

The surface topography describes (1) the degree of roughness that the surface exhibits as well as (2) the orientation of the irregularities on the surface Surface roughness occurs in two principle planes one perpendicular to the surface and one in the plane of the surface The orientation of the irregularities may be either isotropic (without a dominating direction) or anisotropic (a distinct and regular pattern) (Wennerberg *et al* 2003)

Further, surface roughness can be described in terms of amplitude, spatial distribution (spacing) and hybrid parameters

Amplitude parameters (R_a, R_q, R_t, R_z, R_{sk}, R_{ku}) describe the vertical height of irregularities and are determined in both 2D and 3D measurements The same parameters but with letter "S" stands for three dimensional evaluation

Spacing parameters describes the space between the irregularities and are also determined in both 2D (S_m) and 3D (S_{cx}) measurements

Hybrid parameters (S_{dq} and S_{dr}) include information regarding both amplitude and spacing

2.1 Roughening procedures

Implant surface roughness can be obtained in two different ways, *i e*, addition or subtraction In the addition technique, the implant is provided with an extra surface or coating Sintering and plasma-spray coatings are the most frequently used techniques The characteristics of plasma-spray deposited coatings can be influenced by several parameters such as temperature of the plasma, nature of the plasma gas, and particle size and chemical nature of the powder (Herman 1988)

Subtraction is a method whereby the surface of a bulk material is modified Due to chemical or mechanical interaction of this substrate, some parts of the bulk material are pulled off, leaving a rough surface

A common subtraction technique is grit blasting Pitting the surface with grit particles roughens the implant These particles reach the surface with a certain velocity and subtract a small amount of material By varying size of the particles and blasting pressure, the final microroughness can be changed Two types of powder particles are regularly used as blasting material, TiO_2 and Al_2O_3

Acid etching is another subtraction technique to modify the implant surface Depending on the type and concentration of the acid used, the surface will have a high or low roughness value This method can be used in combination with another technique, like grit blasting

Photolithography is a third subtraction technique Photolithography is a texturing technique that incorporates the exposure of radiation-sensitive polymer film coating to a predetermined radiation pattern produced through computer imaging procedures

2.2 Surface roughness and bone healing

Macroscopically, osseous structure is classified according to its density as compact or trabecular bone Bones are composed of four microscopic tissue types woven, lamellar, bundle, and composite bone (Roberts *et al* 1993)

Hulshoff & Jansen (1997) described the initial interface healing around tapered, conical, screw shaped dental implants After 3 days, blood coagulum, primitive bone marrow cells, and undifferentiated inflammatory cells were visible Only few multinucleated giant cells were present After 12 days of implantation, a callus of woven bone was formed, which bridged the existing space between bone trabeculae and implant surface Extensive networks of active osteoblasts were seen Bone formation was not restricted to the interface Trabeculae of the surrounding bone that were not traumatized by drilling also showed an active formation of new bone Still inflammatory cells were seen, though in a lesser extent than after 3 days of implantation After 24 days of implantation, a higher percentage of bone contact was observed Even if the implant apically was not in contact with the original bone, a thin layer of bone was often covering the implant at that site

A new semi quantitative scoring system that discriminated various tissues in contact with the implant was used by Dhert *et al* (1998) in order to evaluate early healing around bone implants They described that the following cellular and tissue response sequences could be discerned

(1) 3 days after implantation, original bone and blood were the main tissues in contact with the implant surface, (2) after 7 days, callus and mesenchymal tissue as well as remodelling lacunae appeared at the interface, (3) after 14 days, osteoid and new lamellar bone were present at the implant surface with a significantly higher fraction of osteoid tissue for HA as compared with TiAlV and Ti, (4) at 28 days, new bone was the main tissue type in contact with the implant surface Recently, Berglundh *et al* (2003) studied early bone healing of solid screw implants provided with the so-called SLA surface topography A U-shaped circumferential trough was prepared within the thread region, but leaving the tip of each pitch of the thread untouched They demonstrated that, initially in this way created wound chamber was occupied with coagulum and granulation tissue, which was subsequently replaced by

a provisional matrix The process of bone formation started during the first week Although, the newly formed bone present at the lateral border of the cut bony bed appeared to be continuous with the parent bone, woven bone was found on the implant surface at a distance from the parent bone This primary bone was replaced by parallel fibered and or/ lamellar bone and marrow Between 1 and 2 weeks, the bone tissue immediately lateral to the pitch region became resorbed and replaced with newly formed viable bone They concluded that osseointegration represents a dynamic process both during its establishment and its maintenance

In various studies, it has been shown that the way in which the body interacts with the implant is affected by the implant surface composition, topography, roughness, and surface energy (Schwartz & Boyan 1994)

In general, the stages of cell-material interaction at the bone-implant interface can be summarized as protein adsorption, cellular adherence, local factor production, proliferation, differentiation, matrix production, and calcification (Schwartz *et al* 1997) In view of this, cell culture experiments can provide evidence for the basic cell material interactions because it offers possibilities to analyze the different steps leading to firm tissue-material contact

The comparison of the behaviour of different cell types on materials shows that they react differently according to surface roughness (Meyle *et al* 1993, Chesmel *et al* 1995, Healy *et al* 1996, Thomas *et al* 1997) Scanning electron microscopic examination of bone cells on materials with various surface roughnesses generally demonstrated that cell spreading and continuous cell layer formation was better on smooth surfaces compared to rough ones (Naji & Harmand 1990, Kieswetter *et al* 1996, Anselme *et al* 2000)

Results of in vitro studies demonstrated also that on rough (sand-blasted, etched and plasma-sprayed) surfaces the metabolic activity of osteoblast-like cells was significantly increased Cells on rough surfaces produced 1 5 to 4 times more PGE_2 and also TGF-β_1 as compared with cultures on plastic and smooth surfaces As a consequence, it was concluded that substrate surface roughness affects cytokine and growth factor production, suggesting that surface roughness may modulate the activity of cells interacting with an implant and therefore affects tissue healing and implant success (Davies 1996, Kieswetter *et al* 1996, von Recum *et al* 1996, Cooper *et al* 1998) In other studies (Boyan *et al* 1998) it was demonstrated that alkaline phosphatase activity and osteocalcin was increased by substrate surface roughness The authors concluded that bone cell response to systemic hormones is modified by rough surfaces. Further, rough titanium surfaces (sandblasting or coating by plasma spraying) were shown to significantly enhance cellular attachment and production of extracellular matrix and subsequent mineralization in vitro (Bowers *et al* 1992, Groessner-Schreiber & Tuan 1992).

Evidently, osteoblast/material interaction depends on the surface aspects of materials that may be described according to their topography, chemistry and surface energy These surface characteristics determine how biological molecules will adsorb to the surface and more particularly determine the orientation of adsorbed molecules (Boyan *et al.* 1996) They also determine the cell behaviour on contact Cells in contact with a surface will first attach, adhere and spread (Anselme 2000). The adhesion strength of osteoblast-like cells was highest on surfaces, which had been plasma-cleaned (Swart *et al.* 1992) In another study it was demonstrated that osteoblasts adhered tightly to and spread on both HA- and Ti-surfaces However, the regulation of cell adhesion to HA was found to be different from that to titanium and it was suggested that Arg-Gly-Asp (RGD)-containing serum proteins might play a major role in regulating the specific adhesion of osteoblasts to HA, and in inducing enhanced cell growth and differentiation (Okamoto *et al* 1998)

Nevertheless, it has to be noticed that clinically, upon implantation the first cells coming into contact with the material are blood cells (monocytes, neutophils), followed by epithelial cells, fibroblasts and bone cells (Meyle, 1999) In view of this, it is known that fibroblast and epithelial cells behave differently if seeded onto smooth or rough titanium surfaces in vitro (Hormia *et al.* 1991; Hormia & Kononen 1994). Surface treatment of titanium and hydroxylapatite did not alter the growth rate of rat epithelial cells Compared with tissue culture polystyrene, the growth on titanium and hydroxylapatite was reduced (Jansen *et al* 1989a & b). On the other hand, macrophages when attached to a rough surface showed bone-resorbing activity and increased PGE_2 release (Murray *et al.* 1989).

Further, many authors have demonstrated in *vitro* studies the occurrence of the so-called contact guidance phenomenon using fibroblasts or epithelial cells. Epithelial cells orient markedly along the axis of 10 μm deep grooves on a titanium-coated implant (Gronowicz & McCarthy 1996). The modification of groove width or groove depth did not affect the cellular orientation (Den Braber *et al* 1995). The contact guidance phenomenon has also been described for osteoblastic cells On smooth surfaces, bone cells were randomly oriented although they were aligned parallel to the direction of the grooves In contrast, they ignored the surface topography on a 0 5 µm grooved surface (Chesmel *et al* 1995)

In vivo it appears that the surface characteristics of an implant, particularly roughness, may control tissue healing and therefore subsequent implant success (Schwartz *et al* 1997, Wennerberg *et al* 1997) The effect of different titanium surface roughness has been tested in numerous in vivo studies utilizing different animal models Therefore, the conclusion that there is sufficient evidence that titanium implants with a roughened surface achieves faster bone integration appears to be justified (Davies 1998)

In general, in *in vivo* animal experiments, the clinical performance of the titanium implants is described on basis of mechanical test and histologic evaluation In most studies, increasing roughness results in increased percentage of bone in contact with the implant (Cordioli *et al* 2000, Novaes *et al* 2002, Zechner *et al* 2003) On the other hand, other studies demonstrated no difference between groups with different surface topographies (Caulier *et al* 1997, Grizon *et al* 2002, London *et al* 2002, Kim *et al* 2003)

The results of mechanical evaluation of bone anchorage, demonstrated that implant surface roughness is important to obtain a superior mechanical fixation of the implant in the surrounding bone (Klokkevold *et al* 1997, Buser *et al* 1998, Gotfredsen *et al* 2000, Klokkevold *et al* 2001) Controversially, some studies showed no statistical significant difference between different rough implants (Vercaigne *et al* 1998, Vercaigne *et al* 2000)

3. Surgical considerations

The majority of oral implant articles focus on the importance of altering implant surfaces to improve clinical results However, the evidence of these changes is based on short-term animal experiments and the finding of more bone or more rapidly invading bone at the interface of the implant (Albrektsson 2001)

An important feature of the osseointegration is the emphasis put on efforts to minimize any damage to the host tissues, by e g contaminants and thermal or surgical trauma The surgical implant procedure is a sensitive technique (Adell *et al* 1981) Inadequate surgical technique is considered one of the causes of implant failure Implant failure may result from inadequate irrigation of the surgical site or from using low torque and excessive drill speed during surgical placement (Ashley *et al* 2003) Also, implant failure can result from excessive temperature elevation in the bone during implant placement, leading to necrosis of the supporting bone around the implant (Eriksson *et al* 1982) Kerawala *et al* (1999) observed that although no relationship existed between drill speed and temperature increase during osseous preparation, the use of integral irrigation, appropriate bur design, and atraumatic surgical technique are important factors for success One of the most important factors identified for implant success was "surgery without compromise in technique" (Block & Kent 1990)

Support for the importance of surgical factors is provided by Bahat (2000), who placed implants in bone of poor quality He concluded that the quality and quantity of bone appeared to have little influence on the success rate, but that surgical techniques are particularly important to the success of osseointegrated implants placed in the posterior maxilla With careful surgical planning and execution, high success rates can be achieved (success rate was 94 4% at 5 to 6 years and 93 4% after 10 years)

Partly in agreement with Bahat, Esposito *et al* (1998a) demonstrated that surgical trauma combined with bone volume and qualities are generally the most important etiological factors for early implant failure Excessive surgical trauma together with an impaired healing ability, premature loading and infection, and insufficient implant stability are likely to be the most common causes of early implant losses (Esposito *et al* 1998b)

Many variations in the surgical technique for the placement of dental implants have been developed since the introduction of implant surgery into clinical practice in combination with different implants system These include variations in the way the recipient bone site is prepared For example, bone compaction before implant insertion (Kold *et al* 2005, Rambla-Ferrer *et al* 2006) or widening of a narrow edentulous alveolar ridge before bone preparation (Chiapasco *et al* 2006, Calvo-Guirado *et al* 2006)

In view of the above mentioned, it has to be emphasized that more research is necessary in order to find evidence for better efficacy of one or the other implantation technique compared to the other

4. Research objectives

As described before, several parameters seem toinfluence the performance of dental implants, amongst them are, implant surface condition, surgical technique at insertion and bone quality/density of the implantation site

From the literature it is known that titanium implants with a roughened surface provide faster bone healing, higher percentage of bone contact and higher resistance to shear (Buser 1999) However, Albrektsson (2001) stated that improvements of the surgical technique seem to be a reliable way of increasing oral implant success

Consequently, we hypothesize that the used surgical technique for implant placement affects the final bone healing and has to be considered as important as the implant surface properties To answer this hypothesis, the following questions were addressed in this thesis

1 Does a higher implant surface roughness lead to a higher bone-to-implant contact?

2 Does a higher implant surface roughness result in a higher implant torque resistance?

3 Is the surgical technique one of the major parameters for the final implant-bone behavior and perhaps more important than implant surface parameters, like roughness and composition?

4 Can a particular surgical technique increase the survival rate of implants?

5 Does the used surgical technique affect the final implant fixation and bone behavior?

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Chapter 2

Implant surface roughness and bone healing: a systematic review

Abstract

A systematic review was performed on studies investigating the effects of implant surface roughness on bone response and implant fixation We searched the literature using MEDLINE from 1953 to 2003 Inclusion criteria were (1) abstracts of animal studies investigating implant surface roughness and bone healing, (2) observations of three-month bone healing, surface topography measurements, and biomechanical tests, (3) provision of data on surface roughness, bone-to-implant contact, and biomechanical test values The literature search revealed 5966 abstracts There were 470, 23, and 14 articles included in the first, second, and third selection steps, respectively Almost all papers showed an enhanced bone-to-implant contact with increasing surface roughness Six comparisons were significantly positive for the relationship of bone-to-implant contact and surface roughness Also, a significant relation was found between push-out strength and surface roughness Unfortunately, the eventually selected studies were too heterogeneous for inference of data Nevertheless, the statistical analysis on the available data provided supportive evidence for a positive relationship between bone-to-implant contact and surface roughness

Introduction

A major parameter for the clinical success of endosseous implant therapy is the formation of a direct contact between implant and surrounding bone The implant-bone response is thought to be influenced by the implant surface topography As a consequence, over the last 20 years, a large number of implant systems with different surface topographies have been introduced The literature on this topic is extensive and continuously increasing (Table 1) However, the claims made in numerous publications about the effect of implant surface roughness on bone response are not as straightforward as suggested For example, there is a lack of agreement in findings in *in vivo* animal experiments, where the clinical performance of micro- roughened titanium implants is described on the basis of mechanical failure tests and histological considerations Some of the studies indicated a tendency for an increase of bone-to-implant contact with increasing roughness of the implant surface (Buser *et al* 1991), while other studies either could not confirm this observation (London *et al* 2002, Novaes *et al* 2002) or could not find any effect at all (Carlsson *et al* 1988, Gotfredsen 1992, Vercaigne *et al* 1998a, 2000a) Also, it has been suggested that only a very specific surface topography with a R_a value between 1 and 1 5 µm provides an optimal surface for bone integration (Wennerberg and Albrektsson 2000)

Various explanations can be given to rationalize the above-mentioned discrepancies in the biologic effect of substrate surface roughness, like small but very relevant differences in surface topography, different animal models, and different surgical techniques Because the utilization of oral implants is increasing, it is essential that clinicians have unequivocal evidence to support claims of alleged benefits of specific morphological characteristics of dental implants (Jokstad *et al* 2003) A thorough meta-analysis of the available literature on this topic would be the most appropriate strategy for achieving this goal Although several meta-analyses have been done so far, none of them addressed animal studies (Cochran 1999, Lee *et al* 2000, Stach and Kohles 2003, Albrektsson and Wennerberg 2004 a, b) Therefore, the aim of the current study was a systematic analyze the data regarding implant surface roughness, to determine its relationship, if any, with bone healing and biomechanical tests

The hypothesis tested in this study was that (1) higher implant surface roughness leads to a higher bone-to-implant contact (BIC), and (2) higher implant surface roughness results in a higher implant torque resistance

Materials & Methods

The major phases in this review were literature search and selection, inclusion / exclusion of papers, extraction of data, and statistical analysis The literature was searched in an electronic database (MEDLINE) for dental articles written in English between 1953 and 2003 The Keyword used was "dental implant" Two independent readers carried out a selection of the references found on the basis of abstracts as published in MEDLINE If no abstract was available in the MEDLINE, the original article was used The emphasis of this first step in the review procedure was on inclusion of references according to the criteria shown in Table 1 Author's names in the papers included in this step were re-checked in MEDLINE and cross-matched with the original list of references to add references that met the inclusion criteria Disagreements were resolved by discussion

The second step of the selection procedure consisted of the reading of the sections "Aim", "Materials & Methods" and "Results" in the articles The same two readers independently selected the blinded papers to be included in this step on the basis of an additional list of selection criteria (Table 1, step 2)

In step three, papers were included that provided surface roughness values, bone-to-implant contact (BIC) and biomechanical test results of the respective test groups in each study Finally, the data of these properties were extracted

For step one and two, the Cohen's Kappa-coefficients were used as a measure of agreement between the readers The principal author undertook step three

For analysis of data, slopes of regression lines (and 95% Confidence Intervals) were used to express the relationship with roughness If only two values for roughness were available, the Student's *t* test was applied, and the slope (and 95% CI) could easily be calculated Slopes were considered to be significant if the 95% CI did not include the value of zero

Table 1 Papers chosen after second selection (in alphabetical order, n = 23), papers remaining after third selection are in italics (n =16) [Complete details of references are listed in the appendix]

Reference	Reason(s) for exclusion
Buser *et al*, 1999	No bone BIC* % mentioned, and healing period not mentioned in the graph
Dhert et al, 1991	
Dhert et al, 1993	
Giaveresi *et al*, 2002	No BIC % (only inside screw threads and 3 best threads)
Gotfredsen *et al*, 1992	Removal torque test without limit and inadequate BIC data
Gotfredsen et al, 1995	
Hallgren et al, 2001a	
Hallgren et al, 2001b	
Hallgren et al, 2003	
Han et al, 1998	
Hulshoff et al, 1997	
Johansson & Albrektsson, 1991	No R_a (only R_z) and no BIC (only 3 best threads)
Johansson *et al*, 1998	No three-months healing data
Muller-Mai *et al*, 1989	No R_a, only R_t used for surface roughness
Rupprecht et al, 2002	
Vercaigne et al, 1998b	
Vercaigne et al, 2000a	
Vercaigne et al, 2000b	
Wennerberg et al, 1995	
Wennerberg et al, 1996a	
Wennerberg et al, 1996b	
Wennerberg *et al*, 1997	No three-months healing data
Wong et al, 1995	

* BIC = bone-to-implant contact, R_a = description of height variation, R_z = average value of absolute heights of 5 highest peaks and 5 deepest valleys, and R_t = maximum peak-to-valley height of profile in assessment length (area)

Results

The MEDLINE literature search resulted in a list of 5966 hits After the first selection step, 470 articles remained, 5496 were excluded The inter-reader agreement (k [kappa] = 0 51 ± 0 03) reflects moderate agreement To check the validity of this procedure, we subjected a random selection of 100 papers out of the 5378 double-negative (both readers excluded them) to the criteria of step two None of the 100 papers was positive

The second step revealed 23 papers fulfilling all criteria of the selection procedure The inter-reader agreement for this step was κ = 1 In total, 447 papers were excluded from further analysis for one or more reasons 324 papers did not describe surface topography, no biomechanical tests were performed in 307 papers, 122 papers did not mention bone-to-implant contact, and 74 papers described studies that did not have the required minimum bone-healing period of three months

In step three, 7 more papers were excluded for reasons mentioned in Table 2 Of the 16 remaining papers, two sets of papers dealt with one and the same study (Dhert *et al* 1991, 1993, Vercaigne *et al* 2000a,b) Consequently, 14 studies (16 papers) remained for inference of data Three studies divided the implant groups either by implant sites (Dhert *et al* 1991,1993, Hallgren *et al* 2003) or presented data based on two different implant designs (Gotfredsen *et al* 1995)

As a result, data of 16 groups of implants were available for statistical analysis All studies investigated the relation between surface roughness and bone-to-implant contact Although most papers described multiple surface roughness descriptors (*i e* , R_a/S_a, R_q/S_q, R_{sk}/S_{sk}, ect), R_a/S_a was the only descriptor common to all papers and therefore was used in the present study as a measure of surface roughness R_a is the two-dimensional (2D) counterpart of the three-dimensional (3D) descriptor S_a Both R_a and S_a reflect the arithmetic mean of the absolute values of the surface point departures from the mean plane within the sampling area (Wennerberg 1996)

Fifteen out of 16 comparisons showed a positive relation between surface roughness and bone-to-implant contact the higher the surface roughness, the higher the percentage bone-to-implant contact (Figs 1a ,2) Six comparisons had a statistical significance, since their slopes were significantly different from zero (Fig 2) The remaining comparisons revealed 9 positive slopes that did not differ significantly from zero, and the negative slope was also not statistically different from zero (Fig 2) Four studies (Wennerberg 1996a, Vercaigne *et al* 2000a,b, Hallgren *et al* 2001a, Rupprecht *et al.* 2002) were not of value, because of extremely large standard errors (SE> 50% BIC/μm), and for this reason were not included in Fig. 2.

With regards to biomechanical testing, 9 papers used a removal torque test to assess the correlation between biomechanical properties and surface roughness and expressed

Table 2 Inclusion and exclusion criteria for the selection of papers in the three selection steps.

Step 1	Include	- Animals' studies, *in vivo* - Studies dealing with implant surface roughness and bone healing - Also, implant surface chemistry and bone healing - Control groups from other studies, even if the test group(s) does not fit with other criteria
	Exclude	- Descriptive studies (*i.e.*, preliminary, case reports, pilot studies, reviews and meta-analyses).
Step 2	Include	- Healing period after implant placed, 3 months or more - Surface roughness parameters measured - Type of surface mentioned (*i.e.*, machined, etched…) - Biomechanical test used - Bone-to-implant contact measured in for separate groups and expressed in percentage - Location of the implantation should be mentioned in the studies - Loading or unloading clearly written in the papers
	Exclude	- Studies not meeting all criteria above for inclusion
Step 3	Include	- Three-months healing period after implant placed - Surface roughness parameters measured (R_a or S_a)[1] - Results of surface examined - Biomechanical test used (RTV[2] or equivalent value) - Bone-to-implant contact measured in all groups
	Exclude	- Studies not meeting all criteria for inclusion

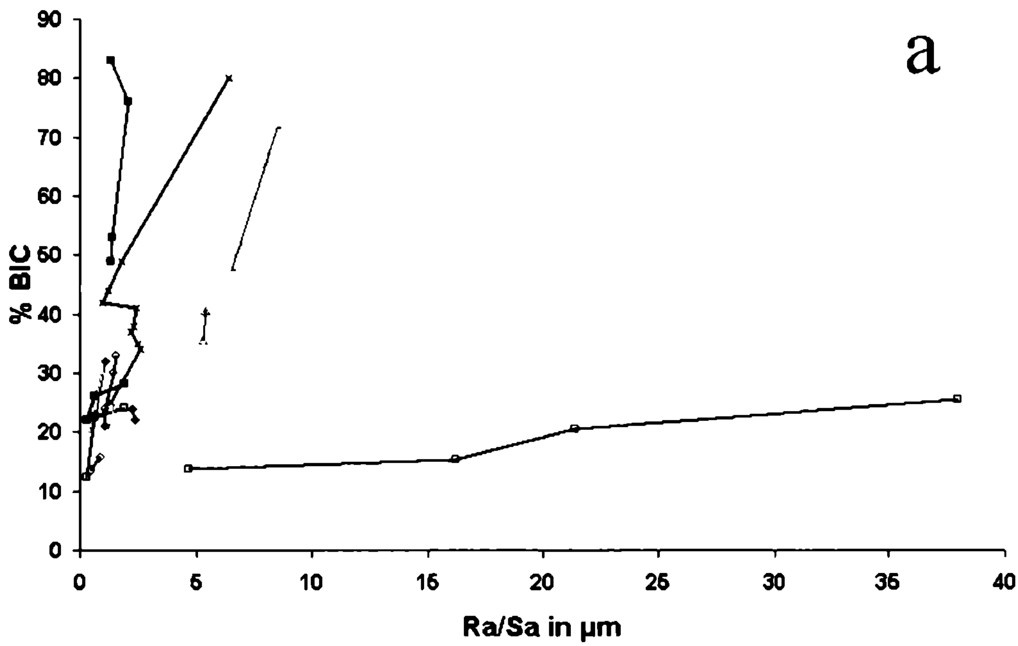
[1] R_a/S_a = Description of height variation.

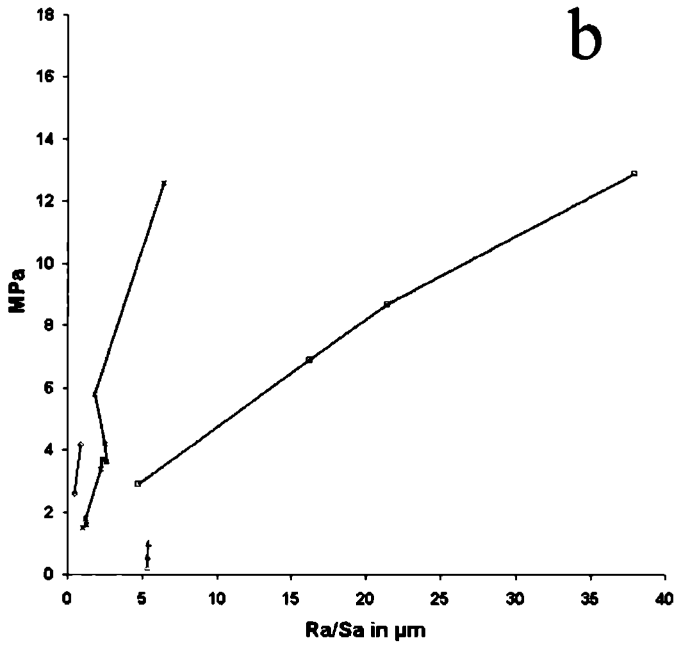
[2] RTV= Removal torque values.

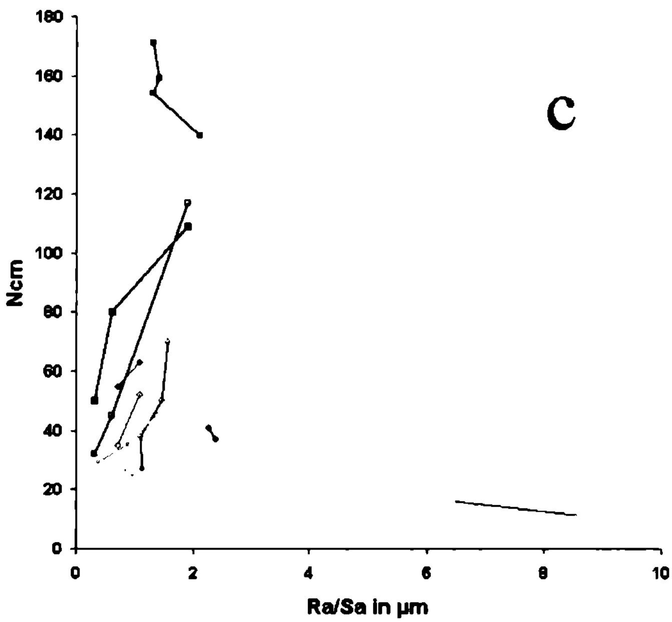
Figure 1 Scatter plots of surface roughness-BIC (a), -push out test (b), and –torque test (c) comparisons. Lines connect data within studies.

[C] = Cylindrical implants; [S] = Screw implants; [F] = implant site in femur; [H] = implant site in humerus.

Dhert 1991+1993[F]
Dhert 1991+1993[H]
Gotfredsen 1995[C]
Gotfredsen 1995[S]
Hallgren 2003
Hallgren 2001(a)
Hallgren 2001(b)
Han 1998
Hulshoff 1997
Rupprecht 2002
Vercaigne 1998(b)
Vercaigne 2000(a+b)
Wennerberg 1995
Wennerberg 1996(a)
Wennerberg 1996(b)
Wong 1995

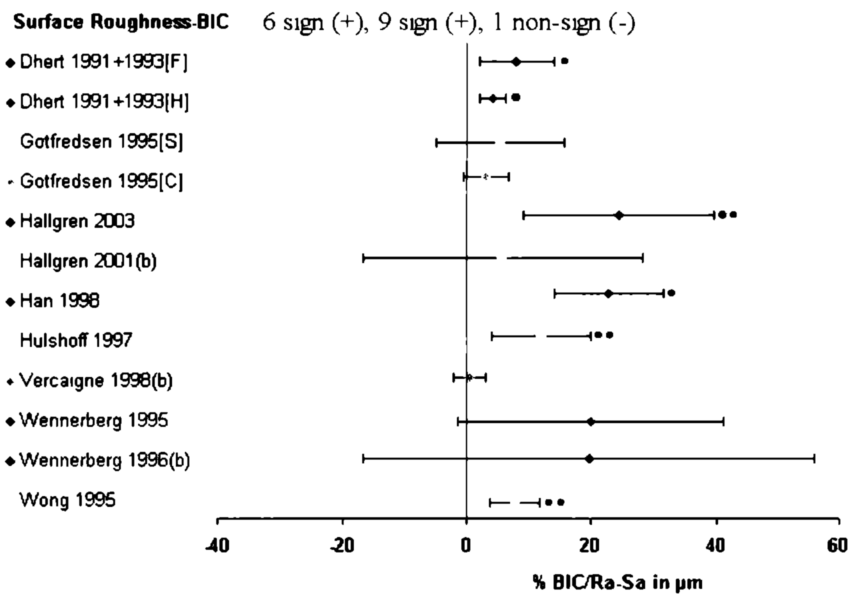


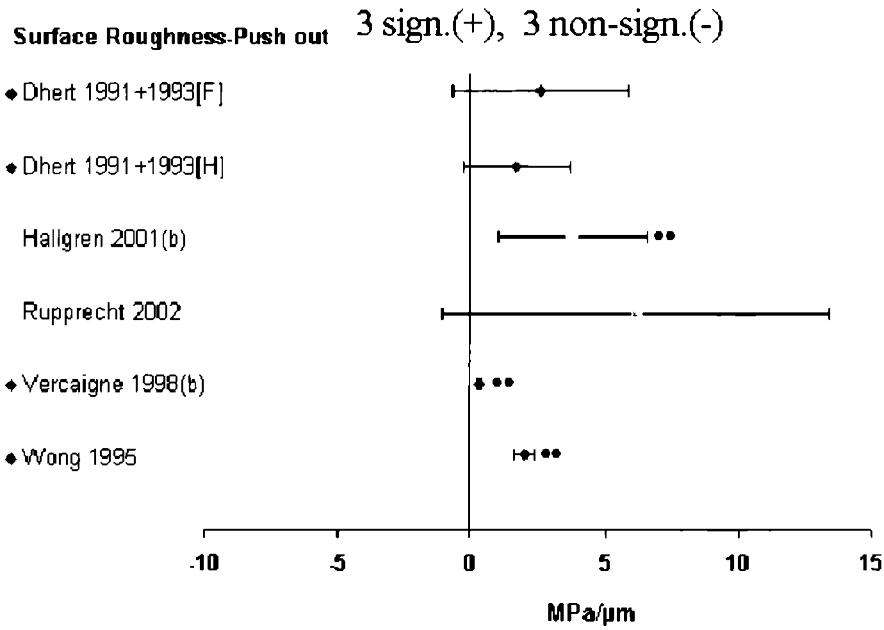

b
MPa
18
16
14
12
10
8
6
4
2
0
0
5
10
15
20
25
30
35
40
Ra/Sa in µm

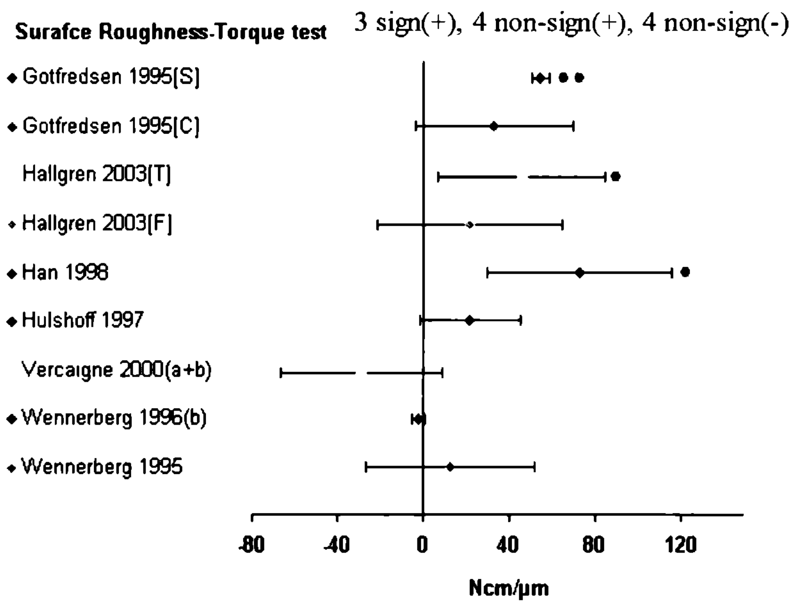

c
Ncm
180
160
140
120
100
80
60
40
20
0
0
2
4
6
8
10
Ra/Sa in µm

the results in Ncm. Five papers described push-out tests and expressed the strengths in MPa. Because the results of the two biomechanical tests are not compatible, two subsets were constructed for further analysis (Fig. 1b, 1c). In all studies that presented data on push-out tests, the push-out strength increased with higher surface roughness values (Fig. 1b). All slopes were positive, of which 3 were significantly different from zero (Fig. 2). In contrast, the relation between surface roughness and torque test values is less clear (Fig. 1c). The slopes in 5 studies revealed a positive relationship (the higher the surface roughness, the higher the torque test value), of which 3 were significantly different from zero (Fig. 2). In contrast, 4 studies produced negative slopes that were not significantly different from zero and 2 of these studies (Wennerberg *et al.* 1996a; Hallgren *et al.* 2001a) did not provide reliable information because of the large standard errors (SE > 100 Nm/μm) and were therefore not included in Fig. 2.

Figure 2 Mean values and 95% Confidence Interval for the slopes of the surface roughness-BIC/torque/push-out test comparisons of the studies evaluated. Asterisks indicate slope-values statistically significant from zero (* = p<0.01; ** = p<0.001).




Surface Roughness-Push out
3 sign.(+), 3 non-sign.(-)
Dhert 1991+1993[F]
Dhert 1991+1993[H]
Hallgren 2001(b)
Rupprecht 2002
Vercaigne 1998(b)
Wong 1995
-10
-5
0
5
10
15
MPa/µm


Surafce Roughness-Torque test
3 sign(+), 4 non-sign(+), 4 non-sign(-)
Gotfredsen 1995[S]
Gotfredsen 1995[C]
Hallgren 2003[T]
Hallgren 2003[F]
Han 1998
Hulshoff 1997
Vercaigne 2000(a+b)
Wennerberg 1996(b)
Wennerberg 1995
-80
-40
0
40
80
120
Ncm/µm

The wide variation in slope values indicates substantial heterogeneity (*i e* , lack of homogeneity) amongst the studies Due to the lack of homogeneity, it is not permissible for the data to be combined for inference Consequently the data from the separate studies cannot be combined, and overall slopes cannot be presented

Discussion

In this study, we attempted, *via* a systematic review, to combine data from animal studies to determine the influence of surface roughness of implants on bone response and implant fixation after 12 weeks of implantation Although, implant surface quality can also be a parameter to facilitate earlier loading of oral implants, the rate of healing was out of the scope of the current review Unfortunately, the studies that were eventually selected were too heterogeneous for inference of the data This heterogeneity may have been caused by differences in measurement methods as well as study designs For example, surface roughness was characterized by different techniques (*i e* , 2D/3D) Moreover, various devices, all of which can introduce unknown variability, were used to determine roughness (Macdonald *et al* 2004) Another variable is the surgical technique used, which is considered an important factor in successful osteogenesis (Sandborn *et al* 1988, Albrektsson 2001), but which was not fully described in all papers So far, surgical technique has been given less attention in evidence-based implantology compared with implant surface characteristics

Furthermore, heterogeneity of data can be caused by variation in the *in vivo* animal model as well as implant location For example, local bone conditions (quantity and quality) vary significantly between various animal species This will have a very serious effect on the results of implant bone response studies It is noteworthy that, of the studies (14) meeting all selection criteria, 9 used rabbits, 4 used goats and one used mini-pigs Despite the observed heterogeneity, this structured analysis summarizes the best current available information on this topic We consider the present blinded review as systematic, reproducible, and one that covered the relevant current literature published in the English language

The selection procedure started with a broad search strategy This was to avoid the risk of exclusion of any paper that might meet our criteria The use of only one data source (MEDLINE) carries a chance of selection bias To overcome this problem, we re-searched by inserting the author's name in MEDLINE This resulted in further identification of 103 papers Inter-reader agreement did not exceed the level of moderate We consider the result (k [kappa] = 0 51 ± 0 03) as acceptable and attributable to the step 1 process of reading only the abstracts

In step 2, where the inter-reader agreement was high (k [kappa] = 1), the entire paper was accessed In most of the included studies, the implant surface topography was characterized by more than one surface roughness parameter (*i e* , R_a/S_a, R_q/S_q, R_{sk}/S_{sk}, ect) However, R_a/S_a was the only parameter that was used in all 14 studies By definition, the R_a- or S_a-value is a good general description of the height variation, but is insensitive to wavelength and occasional high peaks and low valleys (Wennerberg 1996)

Morra *et al* (2003) analyzed the surface composition of 34 different titanium dental implants They reported that surface topography and surface chemistry are intrinsically intertwined and they concluded that surface topography is not the only variable controlling the biological response Yet, despite this shortcoming, we used Ra/Sa as the surface roughness descriptive value to relate bone response with the biomechanical variable

All selected studies dealt with surface roughness and bone-to-implant contact Since about half of the studies showed a significantly increased bone-to-implant contact with a higher surface roughness, the trend for the relationship of surface roughness with bone-to-implant contact is positive In contrast, it has been claimed that only a very narrow range of surface roughness values (*i e* , R_a/S_a value from 1-1 5 µm) positively correlates with increased bone-to-implant contact (Wennerberg and Albrektsson 2000) However, this was not confirmed by the systematic review, because a positive effect on the bone response was seen from R_a/S_a of ~ 0 5 µm up to ~ 8 5 µm Although it is difficult to provide a definite explanation for this discrepancy, we know that surface roughness measurements on oral implants are very complex The different methods used in the various studies can result in different data, which hampers a correct comparison of the results obtained Therefore, a standardized method for measuring and describing surface roughness must be developed

Regarding the interpretation of biomechanical tests, push-out testing has been shown in the literature to be uninterpretable for implant materials with different Young's moduli (Dhert *et al* 1992) The authors in this study focused on the influence of test conditions on the push-out results They demonstrated that comparisons of the bone-implant strength would only give rise to more confusion in interpreting and comparing push-out results Further, the push-out test results showed a stronger relation (Thompson *et al* 1999) between surface roughness and bone bonding strength than the torque test results This relation was seen in the same range of surface roughness values as for the bone-to-implant contact This implies that push-out testing indeed reflects the bone-to-implant response Consequently, removal torque testing might not be the best test for the evaluation of implants fixation or the amount of bone around the implant This suggestion is enhanced by the knowledge that the underlying biomechanical phenomena in torque testing are very complex, *e g* , the shear stress condition at the interface However, the shape or configuration of the implant system is always an additional issue in the selection of a biomechanical test Therefore, push-out testing requires the use of cylindrical implants However, most oral implants have a screw-shaped design Therefore, when there is no other choice than the use of torque testing, bone-to-implant contact measurements should always be performed, and a thorough analysis conducted of the fracture interface after the torque testing, to determine whether the torque failure is indeed caused by failure of the bone-implant interface

In conclusion, the number of publications that met all inclusion criteria was found to be very limited Nevertheless, the statistical analysis on the available data provided supportive evidence for a positive relationship between bone-to-implant contact and surface roughness

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Appendix

Details of Table 2 references

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Chapter 3

The effects of implant surface roughness and surgical technique on implant fixation in an *in vitro* model

Abstract

Objective: The aim of the present study was to determine the relationship between implant surface parameters, surgical approach and initial implant fixation.

Materials and Methods: Sixty tapered, conical, screw-shaped implants with machined or etched surface topography were implanted into the explanted femoral condyle of goats. The implant sites were prepared either by a conventional technique, by undersized preparation, or by the osteotome technique. Peak insertion & removal torque, bone-to-implant contacts (BIC) and morphological bone appearance were assessed by scanning electron microscope (SEM) and microcomputer tomography (micro-CT)

Results: Insertion and removal torque values were significantly higher for etched implants inserted with the undersized technique (115.2 ± 31.1, 102 9 ± 36.4 Ncm) respectively Also, the average BIC value was higher for the etched implants placed with the undersized technique (87.5 ± 5 6), which was statistically significant compared to machined and etched implants inserted by conventional technique.

Conclusion: In conclusion, this study shows that the surgical technique has a decisive effect on implant fixation (represented in this study by installation torque value/removal torque value and histomorphometric evaluation) in trabecular bone Nevertheless, additional *in vivo* studies have to be done to prove the importance of surgical protocol for the final implant-bone response

Introduction

The final clinical success of oral implants is determined by various implant and non-implant-related parameters Implant related parameters are implant shape; implant surface configuration and implant surface composition. Non-implant-related parameters are mainly dealing with the skills of the surgeon, health condition of the patient and final loading protocol of the implant supported prosthetic construction (Albrektsson *et al.* 1981). In view of this, the goal of implant installation is to obtain a good primary stability of the implant in the alveolar jawbone. The establishment of a mechanically stable interface between the implant and bone prevents the development of a fibrous tissue capsule. Subsequently, the implant surface parameters are supposed to stimulate the bone cell reaction resulting in an enhanced healing response and improved implant-bone contact (BIC) In view of this, there are numerous reports that suggest a beneficial effect of implant surface roughness on implant healing and survival (Wennerberg *et al.* 1997, Vercaigne *et al* 2000a, 2000b; Ogawa & Nishimura 2003) Nevertheless, a recently performed systematic review (Shalabi *et al.* 2005) dealing with surface roughened implants in experimental animal studies showed that the effect of surface roughness on oral implant behavior is not as straightforward as claimed Considering that the surgical technique varies between the different studies, the additional effect of surgery on the outcome of a lot of experimental implant studies is perhaps underestimated This suggestion is supported by two recent studies that reported about 93-96% implant success in bone of poor quality and density. In these studies, the original Brånemark implant design was used that was neither surface roughened, oxidized, or coated with hydroxyapatite (HA) Only the surgical routine was changed in that one author preferred to avoid drilling for the full length of the implant and the other drilled more narrow holes than generally recommended (Friberg *et al* 1999 & Bahat 2000). Apparently, such changes in surgical routine can be of paramount importance for clinical success. Still they do not rule out the possibility that hardware alterations may be of some significance as well (Albrektsson 2001). Therefore, due to the controversial results of clinical data, it is currently impossible to determine whether one particular implant is superior to another or if one specific implant design has to be preferred (Puchades-Roman *et al.* 2000; van Steenberghe *et al.* 2000, Gotfredsen & Karlsson 2001, Engquist *et al.* 2002, Astrand *et al* 2004; Wennstrom *et al* 2004)

To obtain a better insight into the above mentioned contradictory data, we postulated the hypothesis that surgical planning and technique are one of the major parameters for the final implant-bone behavior and are perhaps more important than implant surface parameters, like roughness and composition

As part of a consecutive series of studies, the purpose of this paper is to determine the relationship between implant surface parameters, surgical approach and initial implant fixation For this purpose, an *in vitro* experiment was done in which machined and roughened implants were inserted in bone using different surgical protocols The mechanical fixation as well as appearance of the implant-bone interface was evaluated

Materials and Methods

Implants

Sixty tapered, conical, screw-shaped dental implants (Biocomp® Industries, Vught, The Netherlands) were used All implants measured 10 mm in length and had a diameter of 4 6 mm (Figure 1)
The implants were divided into two groups with each a different surface roughness, i e turned, machined and roughened (by grit-blasting and additional acid etching)
A Universal Surface Tester (UST®, Innowep GmbH, Wurzburg, Germany) was used to characterize the surface topographies of the implants This equipment includes a diamond stylus, consisting of a 60° cone, which is moved across a surface with a load of 10 Nm For the topographical analysis of the implants, the roughness (R_a) of the threaded area of three screws from each group were selected at random and measured

Bone specimens

Drilling specimens were collected from the femoral condyle of goats This bone consists mainly of trabecular bone with a thin shell of cortical bone The bone pieces were obtained within 2 h of animal's death and stored on ice at 4°C during transportation from the central animal facility to the laboratory

Figure 1 Machined and etched implants as used in the study.

Implant installation

All bone preparations for implant installation were performed with a very gentle surgical technique by using a dental drill (KaVo EWL Dental GmbH, Biberach, Germany) at a rotational speed of 2000 rpm. The drill was fixed in a drill standard with copious external cooling.

Three different surgical approaches were applied for the installation of the implants:

Approach 1, a press fit technique (according to the protocol of the manufacturer). Drilling started with a rosen drill (diameter 3 mm), a lindemann drill (diameter 2.3 mm for the tip) and pilot drill (diameter 2.55 mm). Subsequently, the hole was widened by a consecutive series of drills, i.e. 3.4, 4, and 4.6 mm drill in diameter. Installation of the implants was done using a Digital® torque gauge instrument (MARK-10 Corporation, New York, NY, USA) in order to measure the in screw torque value.

Approach 2, an under-sized preparation. The same drilling sequence was used as for approach 1, but now the final drill was 4 mm in diameter. Subsequently, the 4.6 mm implant was installed with the torque instrument.

Approach 3, an undersized preparation was made in combination with the use of a spreader (or osteotome) .The drilling was up to a drill with a diameter of 2.55 mm. Then, spreaders with a diameter of 3.4, 4, and 4.6 mm were used for the further preparation of the implant site. The length of the spreaders was 10 mm and each spreader was left for one minute inside the preparation before the next diameter was used. Finally, the implant was installed manually with the torque instrument.

Mechanical testing

Eight specimens of each implant type and surgical approach were prepared to determine torque removal force The torque-measurement device detects and registers the torque necessary to remove the implant

The specimens were placed on a support jig for screw-out measurement This support jig can be adapted in all directions, to put a perpendicular force on the implant For the screw-out test, a slowly increasing torque (displacement 0 5 mm/min) was gradually applied to each implant until loosening When the peak force representing implant loosening was reached, the torque-out procedure was finished

Histological procedures & Histomorphometric evaluation

After implant insertion, two implants of each approach and surface roughness were fixed by immersion in 4% buffered formalin Then, these samples were dehydrated in a graded series of ethanol and embedded in methylmethacrylate About 10-µm-thick sections of the implants and surrounding tissues were prepared using a modified diamond blade sawing microtome technique These sections were made parallel to the long axis of the implant surface The sections were stained with methylene blue and basic fuchsin stains and the amount of bone contact to the implants was determined with help of a light microscope and an image analysis system (Leica Qwin Pro, Wetzlar, Germany)

Scanning electron microscope (SEM)

Following the torque measurement, specimens were fixed and dehydrated by a graded series of ethanol and embedded in methylmethacrylate After polymerization the samples were hemi-sectioned perpendicular on the longitudinal axis of the implants After polishing, the specimens were examined with a SEM (JEOL 6310, Jeol Ltd , Tokyo, Japan) in the backscatter mode in order to analyze the bone appearance after the surgical procedure and the location of the fracture interface after the screw-out test

Micro-computer tomography (micro-CT) evaluation

Also micro-CT equipment (SkyScan-1172, Skyscan n v , Aartselaar, Belgium) was used for 3D analysis of bone deformation as a result of the implant insertion For this procedure, polymeric (MMA) replicas were made of the machined and roughened implants This was done because the use of pure titanium implants results in scattering of X-rays at the bone implant interface, which does not allow a proper analysis of this area MMA resin implants were installed using the same approaches as for the bulk titanium implants (four samples for each approach) After installation, specimens were cut into smaller size and placed in the middle of a cylindrical sample holder High-resolution scanning and cone beam reconstruction were performed with a pixel size of 25 76 µm and a slice thickness of 25 µm The number of slices was set at 472 to cover the entire length of the implant, *i e* 10 3 mm This was in correspondence with the preliminary measured thickness of the bone specimen as measured with calipers and the interactive measurements of the cross-section of the sample The micro-CT software was used to make a 3D-reconstruction from the obtained set of scans

Statistical analysis

Mean values and standard deviations (SD) were calculated One-way Analysis of Variance was used for comparing the differences between groups (ANOVA) All calculations were performed through the use of GraphPad® Instat 3 05 software (GraphPad Software Inc , San Diego, CA, USA) Differences were considered as significant when $p < 0\ 05$ The Dixon outlier test was used to calculate and exclude outlying data from the dataset

Results

Surface roughness measurements of implant surface

Surface topographic evaluation demonstrated that both experimental surfaces differed in surface roughness (Table 1) The machined surface showed an average surface roughness (R_a = 0 45 µm), which was significantly lower than the etched surface (R_a = 1 47 µm) The values for the parameter R_{sk} showed that the two surfaces had a positively skewed surface, the surfaces consisted of more peaks than valleys Although, the data appeared to indicate that the etched implants had a higher R_{sk} mean value, statistical testing revealed that the difference was not significant (Table 1)

Mechanical testing

The results of the torque measurements are listed in Table 2 and depicted in Figure 2 Statistical testing showed that significant differences existed between the various surgical approaches (Table 2) The highest in screw and removal torque (115 2 and 102 9 Ncm respectively) values were always observed for the etched implants installed with approach 2

Table 1 The mean ± sd value of surface roughness parameters

	Machined	Etched	*P* value
R_a	0 45 ± 0 32	1 47 ± 0 54	$p < 0\ 05$
R_q	0 29 ± 0 1	1 82 ± 0 68	$p < 0\ 01$
R_{sk}	0 08 ± 0 35	0 29 ± 0 35	$p > 0\ 05$

Amplitude parameters (Wennerberg)

R_a – the arithmetic mean of the absolute values of the surface departures from a mean plane within the sampling area It is measured in micrometers

R_q – the root mean square value of the surface departures within the sample area It has the statistical signification as the standard deviation of the height distribution

R_{sk} – the measure of the symmetry of surface deviations about the mean plane A negatively skewed surface has more valleys than peaks

Histological and Histomorphometric evaluation

The histological evaluation did not demonstrate a difference in bone contact within the same approaches between the various implants, i e no effect of implant surface properties (machined vs roughened) was seen For all surgical approaches the highest amount of bone-implant contact was observed around the most coronal part of the implants

Further in approach 1 sections the trabecular bone was found to be mainly in contact with the top of the screw threads (Figure 3) A lot of bone debris was seen at the apex of the implants (Figure 4) Occasionally, bone debris was also present in the trabecular voids

Table 2 The mean ± sd (Ncm) of the insertion and removal torque values

Group	**Mean ± sd**	**Comparison**	***P* value**
M press in	81 2 ± 28 4	M press out vs E under out	p <0 001
M press out	50 2 ± 41 9	M under out vs E under out	p <0 01
M under in	93 ± 37 4	M osteo in vs E under in	P <0 01
M under out	54 3 ± 42 7	M osteo out vs E under out	p <0 01
M osteo in	64 3 ± 21 6	E press in vs E under in	p <0 05
M osteo out	48 4 ± 27 9	E under in vs E osteo in	p <0 01
E press in	70 8 ± 25 7	E under out vs E osteo out	p <0 05
E press out	76 6 ± 24 4		
E under in	115 2 ± 31 1		
E under out	102 9 ± 36 4		
E osteo in	66 ± 24 1		
E osteo out	51 ± 23 6		

M = Machined & E = Etched

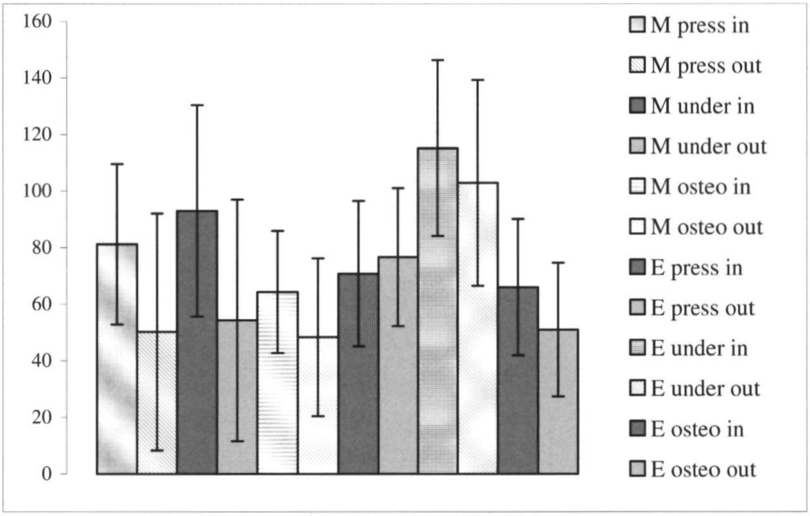
In = in-screw & Out = out-screw

Press = Press fit, Under = Under-sized, Osteo = Osteotome

Approach 2 sections showed that in the trabecular bone area the major part of the implants was in close contact with bone The inner area of almost all screw threads was completely filled with bone Also, a lot of fractured bone particles had penetrated in the trabecular voids (Figure 5)

The light microscopical appearance of approach 3 sections was in between both other approaches Frequently, a lot of bone was observed in the inner area of the screw threads Bone debris, *i e* small bone fragments were seen in the trabecular voids Very occasionally (in two specimens), fracturing of bone trabeculae was observed When present, this only occurred in trabeculae very close to the implant surface Different from the other two approaches, a clear bone condensation was present at the implant apex (Figures 6)

Figure 2: Graph showing the insertion and removal torque values (mean ± SD) as obtained with the various approaches.



M = Machined & E = Etched.

In = in-screw & Out = out-screw.

Press = Press fit, Under = Under-sized, Osteo = Osteotome.

Table 3 Bone implant contact percentage.

Group	**Mean ± sd**	**Comparison**	***P* value**
M press	54.4 ± 10	M press vs E under	p <0.01
M under	71 ± 10.2	M press vs E osteo	p <0.05
M osteo	65.9 ± 8.7	E press vs E under	p <0.001
E press	48.7 ± 2.8	E press vs E osteo	p <0.01
E under	87.5 ± 5.6		
E osteo	77.6 ± 16.6		

M = Machined & E = Etched.

In = in-screw & Out = out-screw.

Press = Press fit, Under = Under-sized, Osteo = Osteotome.

The histomorphometric evaluation showed (Table 3) that there was significantly less bone-to-implant contact for the machined press-fit inserted implants compared with the etched undersized and etched osteotome inserted implants. Statistical analysis also revealed that less bone-to-implant contact existed around etched press fit inserted implants compared with the two other approaches.

Figure 3: Histological section of a roughened implant installed using the press-fit technique. A. the bone trabeculae have only a limited contact with the implant surface (original magnification x 2); B. only occasionally bone debris was present in between the bone trabeculae (original magnification x 7).

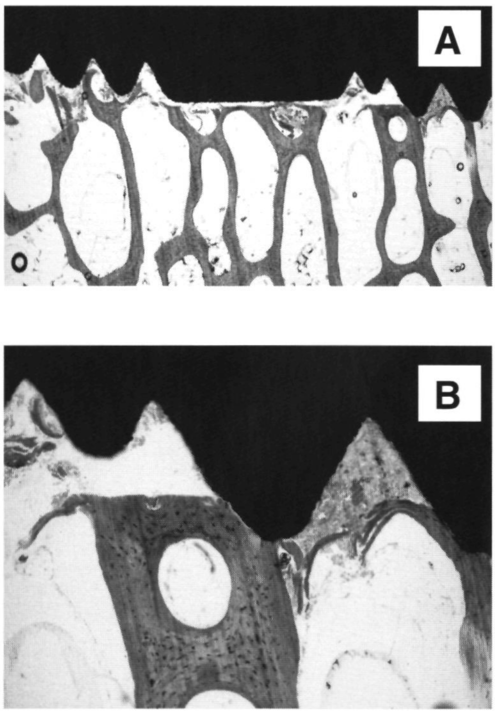


Figure 4: Light micrograph of a roughened implant inserted with the press-fit approach. Fractured bone particles can be seen at the apex of the implant (original magnification x 2).

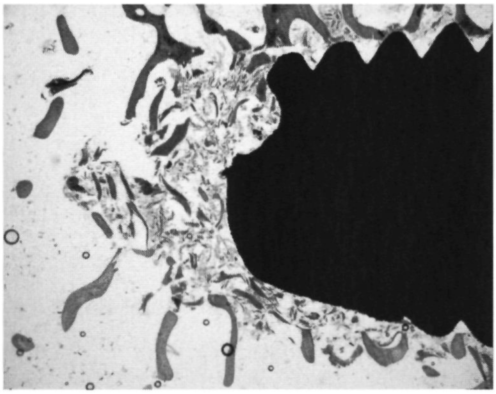


Figure 5: Histological section showing the penetration of bone particles in the trabecular voids after installation of a machined implant using the undersized approach (original magnification x 7).

Figure 6: Light micrograph showing bone densification at the apex of a roughened implant installed with the osteotome approach; A. original magnification x 2; B. original magnification x 7.

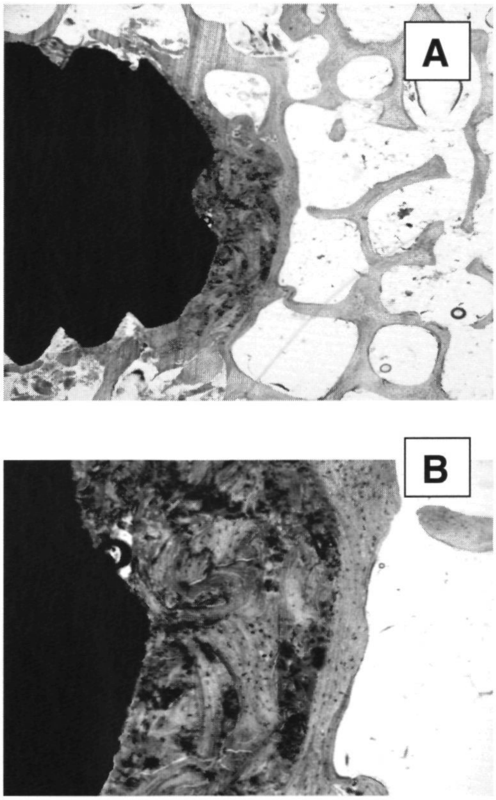


Figure 7: SEM micrograph of an etched implant showing that the majority of screw threads are filled with bone trabecuale when the undersized implant installation approach is used.

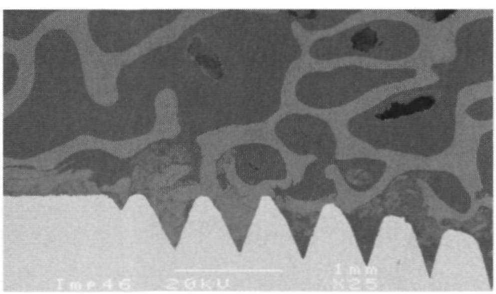
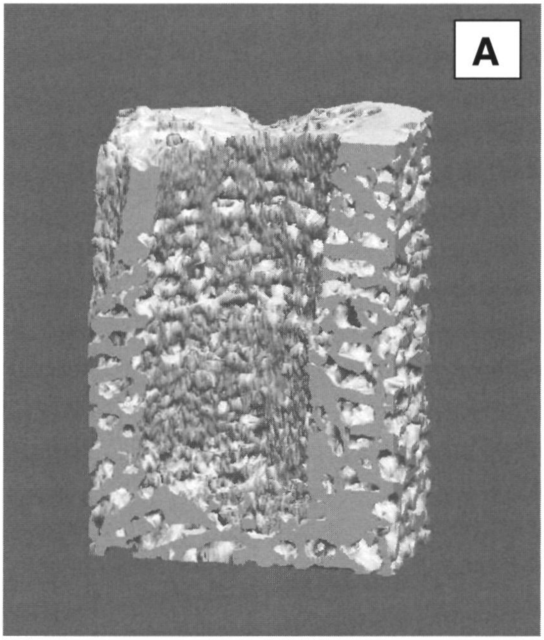
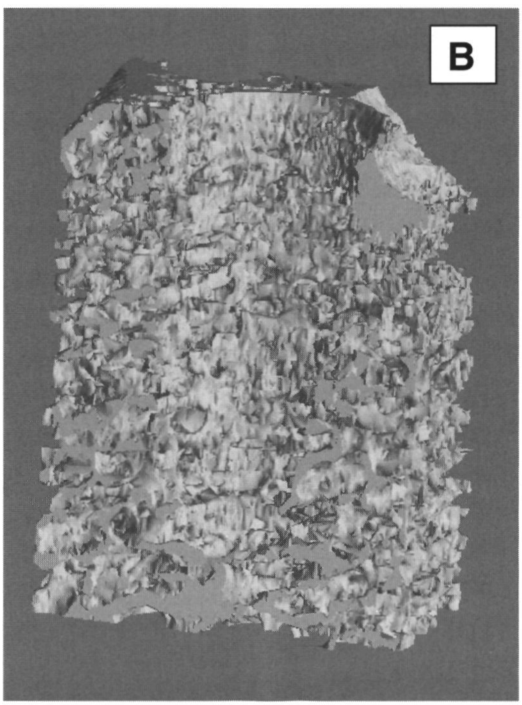
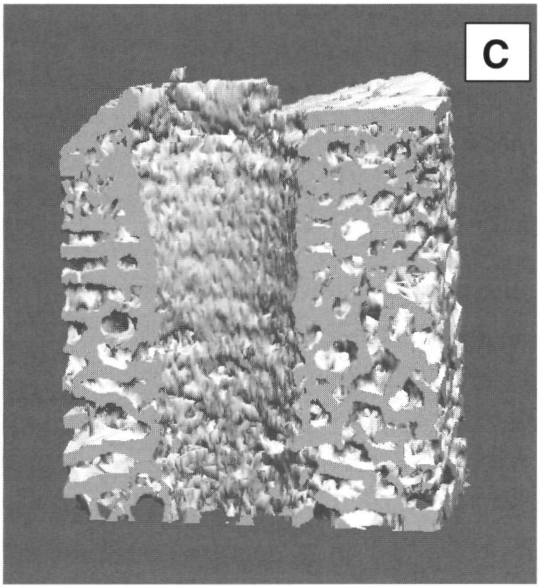


Figure 8: microCT pictures showing the bone appearance after installation of the polymeric implant replica's. A. press-fit approach; B. undersized approach; C. osteotome approach.







SEM

SEM confirmed our light microscopical observations. Similar to the histological sections, in approach 1 trabecular bone was seen to be in contact with only the tips of the screw threads. In approach 2, the majority of the screw threads were filled with bone tissue; a lot of debris was found in the trabecular voids as well as in the inner area of the screw threads (Figure 7). Also in approach 3 some fractured bone trabeculae and debris was observed in the trabecular voids.

MicroCT evaluation

By doing 3D reconstruction of the micro CT images, the three approaches were compared (Fig 8). Similar observations were done as with the light microscopical sectioning and SEM imaging. Approach 1 and 3 resulted in well-defined defects, in which the cavity walls could be recognized very clearly. In approach 3, more bone debris appeared to be present at the coronal side of the bone defect. In approach 2, the defect wall was very difficult to recognize. A lot of small bone particles were present at the implant bone interfaces, which were interspersed in the trabecular bone voids.

Discussion

In the present *in vitro* study we focused on the relationship between implant surface parameters, surgical approach and initial implant fixation Our major finding is that the combination of implant surface roughness with undersized bone drilling results in the highest in- and out-screw values Additionally, histological and microCT analysis showed that undersized drilling gives the highest amount of initial implant-bone contact Combination of all these data indeed confirms that surgical approach has a high impact on the stability and fixation of oral implants This corroborates with a recent study of Buchter *et al* 2003, who also evaluated *in vitro* implant stability of microrough implants inserted into the mandibular bone of minipigs by using a conventional burr technique, burr technique with additional thread cutting and osteotome technique Resonance frequency analysis and removal torque were significantly better for the conventional burr technique compared with the osteotome technique Our data appear to reduce the benefit of the osteotome technique for the installation of oral implants in bone of low density However, we have to notice that the "experimental" osteotome technique as used by us deviates from the original method as described by Summers (1994 a, b & c), who did not use any pre-drilling at all This might explain the lack of initially increased fixation in our study We have to notice that the use of osteotomes is complex and requires additional training and skills from the surgeon A proper orientation of the osteotome instrument is essential for the final shape of the created hole and the fit of the implant For example, jiggling of the instrument during the bone densification procedure has to be prevented, because this can result in extensive widening of the hole in the apical implant area causing decreased implant fixation Further, a recent study of Buchter *et al* (2005) failed also to show a beneficial effect of the osteotome technique on the initial stability of implants, who claimed that this is due to the occurrence of microfractures in the peri-implant bone Despite the agreement in results, this kind of microfracturing was not a constant observation in our histological sections, because it only occurred in a very limited way in only two of the samples

Considering our findings also some comments have to be made on the final biological effect of implant surface morphology vs surgical approach Szmuckler-Moncler *et al* (2004 a & b) stated that it is bone interlocking at the interface that maintains the biological properties of textured surfaces, rather than a strong implant fixation per se and the pits carved during the etching process have a bone-interlocking capacity Subsequently, osteogenesis at the bone-implant interface is supposed to be influenced by various mechanisms, including (1) encouragement of endogenous expression of growth factors and cytokines by osteoblasts (Mustafa *et al* 2002), (2) lower stimulation of osteocytes (the mechanoreceptor cell of bone), and (3) increased adhesion of monocytes/macrophages as well as blood platelets and their secretory profile (Park & Davies 2000, Park *et al* 2001, Soskolne *et al* 2002, Takebe *et al* 2003). Recently, it has even been speculated that the bone healing events around implants follow a biological sequence that is not influenced to a great extent by the implant surface microtopography (Abrahamsson *et al* 2004) Only the final outcome of the healing process would be determined by the implant surface texture, whereby microrough surfaces have to be considered as "osteophilic" The histology and microCT results of the current study leave space for a completely different explanation for increased bone formation Due to the undersized and osteotome approach, a lot of small bone fragments are created and pressed in between the trabecular voids and in between the screw threads during implant installation These bone fragments behave like a kind of autograft and can induce new bone formation It can even be suggested that rough implant surfaces are more prone to adhesion of the bone fragments than machined implant surfaces resulting in an increased bone formation Follow-up in vivo studies have to proof this hypothesis

Finally, it is well known that the implantation of an implant in an undersized implant socket alters the mechanical stresses in the peri-implant area in a significant manner compared with a press-fit inserted implant (Widmer *et al* 1997, Taylor *et al* 1998, Skalak & Zhao 2000) In the present study, the mismatch between implant and drill hole diameter was 0 6 mm This contributed to the increased in- and out-screw values compared with the press-fit inserted roughened implants Nevertheless, we do not know the magnitude of the stress as generated due to this specific size of mismatch This lack of knowledge is significant, because high bone stresses can lead to increased bone remodeling and bone loss (Brunski 2003, Kitamura *et al* 2004) All advices about size of the drill hole implant diameter and specific bone characteristics of the implantation site appear to be based on empirical experiences and lack clear scientific support Therefore, studies have to be performed to the most optimal difference in diameter between drill holes and implant diameter and the subsequent biomechanical adaptation to stress (Hansson 2003 & 2000)

In conclusion, this study shows that the surgical technique has a decisive effect on implant fixation (represented in this study by ITV/RTV and histomorphometric evaluation) in trabecular bone. Nevertheless, additional *in vivo* studies have to be done to prove the importance of surgical protocol for the final implant-bone response.

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Chapter 4

A meta-analysis of clinical studies to estimate the 4.5 year survival rate of implants inserted with the osteotome technique

Abstract

Objective: To estimate the survival rate of implants inserted with osteotome technique by means of a systematic review.

Materials and Methods: The literature was searched using MEDLINE from 1953 to 2005. Inclusion criteria were: (1) clinical studies or clinical reports investigating the osteotome technique for dental implantation and (2) control or test group(s) from clinical study or clinical report, even if the other group(s) did not fit with other criteria. By pooling the data of the included studies, overall Kaplan-Meier survival curves were constructed for the periods before (S_u = survival of implants before loading) and after loading (S_l = survival of implants after loading).

Results: The literature search revealed 164 hits. After two selection steps 5 studies were considered suitable for inclusion. The combined data of 349 implants revealed survival probabilities of 98% (CI: 97.2% - 100%) until loading and 99% (CI: 94% - 100%) after 56 months of loading, respectively. At the end of the observation period 41 implants (18 patients) were still at risk.

Conclusion: The outcome of dental implantation using the osteotome technique in terms of the clinical performance of the implant survival probability seems to be similar to the survival of implants placed by the conventional implantation technique.

Introduction

Over the years, a large number of different implant systems has been introduced with substantial variations in drilling equipment Amongst others, surgical technique is considered to be one of the factors of importance for successful oseointegration of dental implants (Puchades-Roman *et al* 2000, Van Steenberghe *et al* 2000, Gotfredsen & Karlsson 2001, Engquist *et al* 2002, Astrand *et al* 2004, Wennstrom *et al* 2004) Biological failures of oral implants have been associated with bone quality and the degree of surgical trauma (Esposito *et al* a & b)

One of the surgical techniques that has been introduced is the osteotome technique This technique and the instruments used to perform it are defined in the literature with different terms Tatum (1986) designed a set of 'socket formers', which is actually a series of graduated wedges According to the author, these formers can be used to aid in the socket preparation by means of progressive compression of bone and will in this way form the internal configuration of the socket (Tatum 1986)

Later, Summers (1994) was the first to present a complete implant site preparation technique, in which the bone is also not removed but compressed and called it 'osteotome technique' The objective of this technique is to maintain, if possible, all of the existing maxillary bone by pushing the bone aside with - according to the author - "minimal trauma while developing an accurately shaped osteotomy" (Summers 1994)

When reviewing the literature few data were found on the predictability of osteotome technique without additional sinus elevation or ridge expansion (Berengo *et al* 2004, Bragger *et al* 2004, Deporter *et al* 2005, Leblebicioglu *et al* 2005) It appears that in the majority of clinical studies, the osteotome technique was done in combination with sinus floor elevation (SFE) or guided bone regeneration (GBR)

The main purpose of the osteotome technique is to form a denser bone area around the prepared site, thus enhancing the effective bone quality around the implant The healing process after the implantation is not completely clear For instance, the magnitude of forces and the amount of heat generated by 'hammering' the implant site with an osteotome as well as the role that these features play in the healing process are unknown

During the last few years, in vitro models have been used to prove the efficacy of the osteotome technique For example, Buchter *et al* (2003) showed statistically significant higher removal torque values for conventional technique compared to osteotome while Shalabi *et al* (2006) showed only a significant difference between osteotome technique and a so-called under-sized preparation technique, where diameter of implant bed is smaller than the implant diameter; removal torque values were 51 and 103Ncm respectively.

Besides in vitro studies, also several in vivo animal studies have been done. Some of these experiments showed statistically significant removal torque values and bone ratio after 28 days healing for conventional techniques compared to the osteotome technique (Buchter *et al.* 2005 a & b). Nkenke *et al,* 2002 found a statistically significant increase in bone-to-implant contact for osteotome technique after 2 and 4 weeks healing. At 8 weeks, this significant difference no longer existed compared to conventional technique. Also, immediately loaded implants installed with the osteotome technique performed the same as implants subjected to an unloaded healing period prior to loading. No statistical difference in bone-to-implant contact was observed between the two approaches (Nkenke *et al.* 2005 a & b).

Evidently, the currently available experimental data do not provide a clear answer on the final worth of the osteotome technique. On the other hand, it is also known that in vitro as well as in vivo animal data are very difficult to extrapolate to the human clinical situation. This is caused by discrepancies in e.g. loading conditions, bone density, healing time, etc. Fortunately, also several clinical studies have been done using the osteotome technique for the installation of oral implants in the upper jaw of patients. Consequently, the aim of this study was to systematically review the data from reported clinical studies regarding the osteotome technique with the purpose to estimate an overall survival rate of implants by means of a meta-analysis.

Materials & Methods

The major phases in this review were: literature search and selection, inclusion / exclusion of papers, extraction of data, and statistical analysis. The literature was searched with an electronic database (MEDLINE) with year limits 1953 to 2005. The last electronic search was conducted on December 2005. The Keyword used was "osteotome". Two independent readers carried out a selection of the references found on the basis of abstracts as published in MEDLINE. If no abstract was available in the MEDLINE, the original article was used. The emphasis of this first step in the review procedure was on inclusion of references using the criteria shown in Table 1. Disagreements were resolved by discussion.

In the second step, the two readers selected articles on basis of an additional list of selection criteria (Table 1, step 2). Next, the reference lists of included papers were checked by hand and cross-matched with the original list of references with the purpose to add possible overlooked papers meeting the inclusion criteria. The selection procedure was completed by independent reading (two readers) of the aims of the studies and the Materials and Methods, and Results sections of the articles.
Cohen's Kappa-coefficients were used as a measure of agreement between the two readers for both selection steps.
Overall cumulative Kaplan-Meier survival curves were constructed for the periods before (S_u = survival of implants before loading) and after loading (S_l = survival of implants after loading). The end point of S_u was used as the starting point of S_l (S_l = 100%). Standard errors (S.E.) were computed with the Greenwood formula and the confidence intervals with ± 2 * Standard errors. Implants that did not fail at the end of a study observation period were considered as censored observations.
Survival data from the selected papers were only extracted and used for inference when it was described that the osteotome technique was used for implant site preparation with or without sinus floor elevation. Data from articles in which this technique was used for sinus floor elevation only, were not included (i.e. Diserens *et al.* 2005; Khatibolou 2005 and Li 2005).
Mainly, the description of the osteotome technique by Summers (1994) was applied to the selected studies, which reads as; "a complete implant site preparation technique, in which the bone is also not removed but compressed". Only in one selected study another surgical approach was applied consisting of the use of a calibrated trephine drill followed by an osteotome (Fugazzotto 2002).

Table 1 In- and exclusion criteria for selecting papers in two selection steps.

Step 1	Include	- Studies dealing with dental implant & osteotome technique; - Control groups from other studies, even if the test group(s) is not fit with other criteria;
	Exclude	- Descriptive studies (i.e. preliminary, case reports, pilot studies). - Systematic reviews
Step 2	Include	- Clinical studies or clinical reports used "osteotome technique" with dental implants; - Osteotome technique that used for implant site preparation with or without sinus floor elevation.

Results

The MEDLINE literature search resulted in 164 hits After the first selection step, 13 articles remained, 151 were excluded (inter-reader agreement k=0 74 ± 0 09) The second step revealed five papers fulfilling the inclusion criteria (inter-reader agreement k=0 84 ± 0 14) Eight papers were excluded in this step three studies were explanatory & illustrative, three presented in vivo animal studies, one described an in vitro study, and one clinical study investigated implants placed in regenerated bone The hand search did not reveal additional studies to be included (Table 2)

Although the selected studies showed a substantial variation in study characteristics and differences in reporting quality (Table 3), they provided sufficient information for statistical analysis The five studies used the osteotome technique as defined, therefore all data were used for the construction of the cumulative overall survival curve Since all studies presented range follow-up times, only mean follow-up periods could be used as censoring time End points of S_u (time until loading) and S_l (after 56 months) were respectively 98% (CI 97 2% - 100%) and 99% (CI 94% - 100%) (Figure 1 & Table 4, 5, 6)

Table 2 Papers selected after first selection (in alphabetic order, n=13), papers remaining after second selection are presented in *italics* (n=5)

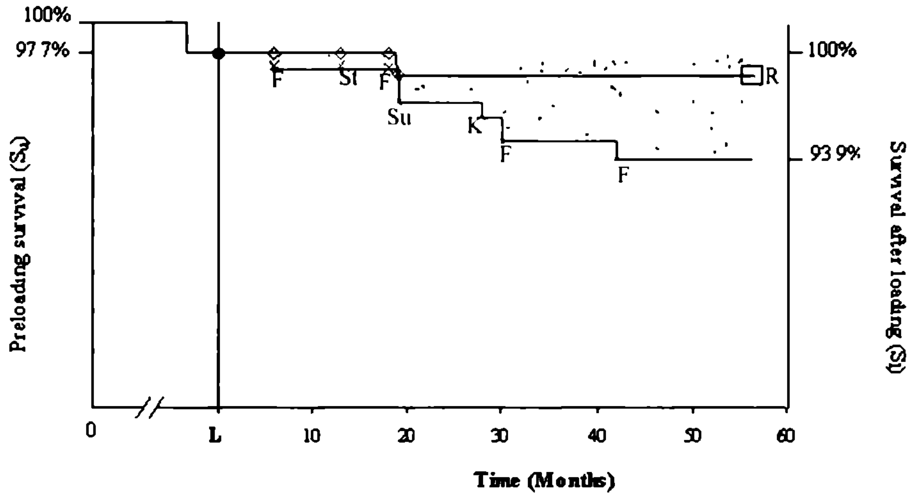
Reference	Reason(s) for exclusion
Barabolia 1972	explanatory & illustrative study
Buchter *et al* 2005	in vivo animal study
Buchter *et al* 2003	in vitro study
Flanagan 2002	explanatory & illustrative study
Fugazzotto 2002	-
Fugazzotto & De 2002	implants placed in regenerated bone
Hahn 1999	explanatory & illustrative study
Komarnyckyj & London 1998	-
Nkenke *et al* 2005	in vivo animal study
Nkenke *et al* 2002	in vivo animal study
Rodoni et al 2005	-
Strietzel et al 2002	-
Summers 1994	-

Table 3 Relevant data of the selected clinical studies used osteotome technique

Data	**Fugazotto, 2002**	**Komarnyckyj & London, 1998**	**Rodoni *et al*, 2005**	**Strietzel *et al*, 2002**	**Summers, 1996**
Prospective/ Retrospective	Retrospective	Prospective	Retrospective	Retrospective	Clinical report
Patients selection criteria given	Yes	Yes	No	No	No
Patients	103	16	48 (18)*	22	55
Male/Female	42m 40 8% 61w 59 2%	NA	25m (7)* 23w (11)*	10m 12w	NA
Implants	116	43	134 (18)*	22→12*	143
Implant system	Innovations (3i) Straumann (ITI)	Straumann(ITI)	Branemark+3i	3i+Friadent	Microvent + Inegral + Hexcylinder
Implant surface	NA	TPS	(Turned) Machined	NA	HA+TPS
# Operators	1	NA	2	NA	NA
Technique according to definition	Yes	Yes	Yes	Yes	-
Bone type	NA	III+IV	NA	II+III	IV
Implants length (mm)	NA	NA	10 11 5, 13, 15	NA	≥ 13
With GBR	With + without	With + without	With	NA	NA
With SE	With	With + without	With	NA	NA
Postoperative management	Described	Described	NA	NA	NA
Healing period	6-12 weeks	≥ 9 months	6months	6months	≥ 8months
Loading time (Months)	0-12→ 31implants 13-24 → 43 25-36 → 29 37-48 → 11	9months-4years	9-80	3-12	11-27
Loading type	Single crown, fixed PD, abutment	NA	NA	NA	NA
Reasons for failure/removal given	No	Yes	NA	Yes	No
Complication described	3sites	1 patient	NA	3 patients	1 implants
Implants failure	2	2	0	2	2

( )* = number of patients with osteotome technique
12 = only 12 implants loaded , TPS = titanium plasma sprayed,
HA = hydroxy abatite, GBR= guided bone regeneration, SE= sinus elevation, Fixed PD = fixed partial denture, NA = not available

Figure 1 Survival probabilities of the implants with 95% confidence interval (CI).



The letters in the graph indicate the studies as included for the meta-analysis:

F= Fugazotto, 2002 (four groups divided according to different loading time period as in the original article).

K= Komarnyckyj & London, 1998.

R= Rodoni *et al*, 2005.

St= Strietzel *et al*, 2002.

Su= Summers, 1996.

● Endpoint of preloading period (S_u) (97.7% survival; healing period minimum 6 weeks) and starting point of loading (S_l) (numbers at risk = 349).

□ Endpoint of loading period (98.8% survival, numbers at risk = 41).

__ Confidence interval.

—— Lower confidence interval (end point 93.9% survival).

Table 4 Number of implant at risk and 95% confidence interval (CI) censoring time after loading.

studies	Months	Implants at risk	95% CI
	0	349	0
Fugazotto 2002	6	318	(0.99;1)
Strietzel *et al.* 2002	13	306	(0.99;1)
Fugazotto 2002	18	263	(0.99;1)
Summers 1996	19	122	(0.97;0.99)
Komarnyckyj & London 1998	28	81	(0.96;0.99)
Fugazotto 2002	30	52	(0.95;0.99)
Fugazotto 2002	42	41	(0.94;0.99)
Rodoni *et al.* 2005	56	41	(0.94;0.99)

Discussion

The current study, deals with a systematic review, where data from clinical studies were combined in order to determine an overall survival rate of dental implants inserted by the osteotome technique.

The selection procedure started with a broad search strategy. The use of only one data source (MEDLINE) carries a chance of selection bias. To overcome this problem, the reference lists of included articles were hand searched. Since no additional papers were found that met the inclusion criteria, it was considered unnecessary to apply other databases.

All selected clinical studies except one used the osteotome technique as described by Summers (1994). Fugazotto (2002) described the use of a calibrated trephine bur in the first step in the procedure, mentioning that this method is less traumatic and disconcerting to the patient compared to repeated malleting. Next, a calibrated osteotome corresponding to the diameter of the trephine preparation was used to implode the trephined bone core in the direction of the sinus floor.

Table 5 Details of implant failure of selected studies.

Data	**Fugazotto 2002**	**Komarnyckyj & London 1998**	**Rodoni *et al.* 2005**	**Strietzel *et al.* 2002**	**Summers 1996**
# Implants	116	43	134	22	143
# Implants used for osteotome technique	116	43	18	22	143
# Implants failed before loading	2 (time of abutment placement)	2→ at abutment placement/both replaced	-	2	2 →one during abutment connection, second/infection
# Implants failed after loading	No failure	No failure	-	No failure	3 (treated)
Implants risk period	31implants for 6months 43 for 18mons 29 for 30mons 11 for 42mons	43 implants for 28 months	18 implants for 44 months	12 implants for 13months	143 implants for 19 months
Mean follow-up (months) time=censoring	6, 18, 30, 42	28	56	13	19
# Implants excluded by author (reason)	No	No	Only one implant from each patient included for statistical analysis (23 excluded)	12-evaluated 8-dropped out (not available for follow up)	No

Table 6 Steps of surgical technique for included studies

Data	**Fugazotto 2002**	**Komarnyckyj & London 1998**	**Rodoni *et al.* 2005**	**Strietzel *et al.* 2002**	**Summers 1996**
1	500 rpm (trephine)	Twist drill Ø 2mm	Not described in detail	Pilot drilling	See text detail
2	Osteotome	Osteotome 1+2		Osteotomes	
3	Self-tapping Ø 3 75 or 4	Ø 3 5 dilator		Or Bone condenser (Friadent)	
4	Or Non-self-tapping Ø 4 1	Osteotome 3, SE cases		Implant	
5	Or Non-self-tapping Ø 4 8	Implant			

Finally, the implant site preparation was completed utilizing sequentially sized osteotomes According to the author, the use of a trephine before the osteotome reduces the loss of significant amounts of bone compared with the use of spiral pilot drills Although this surgical technique is considered to be substantially different from the techniques described in the other selected papers, it is still within the lines of the definition used in this study for osteotome technique Further, it has to be noticed that in the Fugazotto study two different implant systems were used and four different loading groups However, the results were only reported in relation to loading and the data were not handled independently for implant system

Unfortunately, no systematic reviews are available, which deal exclusively with maxillary implants Therefore, the results of the current meta-analysis were compared with other clinical reviews, which contained mixed populations (i e both mandibular and maxillary implants) The comparison indicated that the present finding is within the range of those found in other reviews, in which different implant systems using conventional dental implantation techniques were evaluated (Creugers *et al* 2000, Eckert *et al* 2005) Eckert (2005) estimated an overall 5-year survival rate of 96% (CI 93- 98%) for the pooled data of 17 articles (in total 7,398 implants) and found no differences between implant survivals of the evaluated systems However, since the present meta-analysis, as well as the outcomes of the above-mentioned reviews, are partially based on cohort studies and case series and not on randomized clinical trials (RCTs) only, direct comparison of efficacies is not permitted A recently published systematic review on RCTs only provided evidence on the efficacy of different implant systems (Esposito *et al* 2005), but no data regarding the osteotome technique were included Moreover, the outcomes were presented in relative-risk ratios rather than in survival probabilities, so comparison is actually impossible Although the reviews mentioned above (Creugers *et al* 2000, Eckert *et al* 2005) failed to provide evidence regarding efficacy, the information regarding clinical performance in terms of survival may be considered as evidence for prognosis (Creugers & Kreulen 2003, Phillips *et al* 2001) It therefore seems that that the prognosis of implants placed in the unfavorable maxillary sinus region as estimated in the present study can meet the prognosis of the mixed implant populations that were involved in the Eckert study (in the included studies a substantial number of implants were placed in the mandible, which is known to be a more favorable site for implantation) (Lindquist *et al* 1996, Arvidson *et al* 1998, Scheller *et al* 1998, Polizzi *et al* 1999, Cooper *et al* 2002)

Whereas the present study was investigating the clinical performance of the osteotome technique for implant site preparation, another recent meta-analysis evaluated the survival of dental implantation following sinus floor elevation with osteotomes (Emmerich & Stappert 2005) Comparison of these two reviews reveals that the survival probabilities again were similar The sets of studies included in these meta-analyses had one common primary study, which is the above mentioned study that includes sinus-elevation by means of reallocation of a trephined bone core (Fugazotto, 2002) In another systematic review, which evaluated implants placed in grafted maxillary sinus sites (Del Fabbro 2004), the survival probability after observation periods of 3 years was calculated to be 88 5% for implants with autogenous bone grafts and 95 6% when bone substitutes were used to build up the implant sites

In conclusion, for the period investigated, the prognosis of implants inserted by osteotome technique as computed in this study seems to be similar to published data of implants that are inserted by conventional drilling technique Nevertheless, it has to be emphasized that no RCTS is available that deals with just maxillary implants Consequently, the performance of such a trial has to be recommended in order to find evidence for better efficacy of one or the other implantation technique compared to the other

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Chapter 5

A mechanical evaluation of implants placed with different surgical techniques into the trabecular bone of goats

Abstract

Objective: The aim of the study was to assess the effects of surgical technique and implant surface roughness on implant fixation

Materials and Methods: A total of 48 screw implants with machined or etched surface topographies were placed into the femoral condyles of goats The implant sites were prepared either by a conventional technique, by under-sized preparation, or by the osteotome technique Bone tissue responses were evaluated after 12 weeks of healing by removal torque testing and histologic analysis using scanning electron microscope (SEM)

Results: The cumulative removal torque value of the etched implants placed with the undersized technique (98 ± 29Ncm) was higher (50 ± 35Ncm) to a level of statistical significance than machined surface implants placed by the osteotome technique SEM evaluation showed that all implants showed interfacial bone contact The torque test resulted in fracture at the bone-implant interface for all experimental conditions

Conclusion: The installation of etched implants using an undersized preparation of the implant bed resulted in superior bonding strength with the surrounding bone at 12 weeks postoperative Evidently, the undersized preparation technique improved the early fixation of oral implants in this study

Introduction

The long-term clinical efficacy of dental implants requires the establishment of a mechanically stable interface with complete apposition between the bone tissue and implant surface without an intervening fibrous tissue layer.

Besides implant surface chemical composition, surface roughness has been shown to be an important parameter in order to improve the bone tissue integration of dental implant (Albrektsson & Wennerberg 2004). Various subtraction as well as addition techniques have already been used to modify the implant surface topography, such as grit-blasting, acid-etching and plasma-spraying (Lincks *et al.* 1998; Castellani *et al.* 1999; Perrin *et al.* 2002; Galli *et al.* 2005). Nevertheless, contradictory results have been obtained, depending on the roughness amplitude and the method used to produce the surface roughness (Vercaigne 1998 a &b).

In addition to implant surface roughness, the surgical technique used for implant placement can have a major impact on initial implant stability (Block & Kent 1990). One surgical technique used to increase initial implant stability in low-density bone is to prepare an implant receptor site that is smaller in diameter than the implant to be placed. In this way, an osteocompressive fit between the implant surface and bone bed is achieved. Implant surface roughness can also affect interfacial shear stress resulting in an increased resistance to loading (Skalak & Zhao 2000 a and b). However, a drawback of all drilling techniques is that bone tissue is sacrificed during the drilling process. This shortcoming is exacerbated in situations where limited bone or bone of lesser density is available. In view of this, the osteotome technique was introduced to increase the primary stability of dental implants (Summers 1994). This technique consists of first preparing a small-sized pilot hole, then compressing the bone tissue laterally and apically with a spreader or implant-shaped instrument. The goal of this technique is to replace the implant with a high degree of stability without additional bone removal, which is theoretically believed to improve final bone healing (Skalak & Zhao 2000; Rosenlicht 2002; Le Gall 2004). This technique may hold promise for implants placed in low-density trabecular bone, e.g. as present in the upper jaw; however, at the moment only a very limited number of experimental studies are available to support this suggestion about the efficacy of the osteotome technique (Nkenke *et al.* 2002 and 2005; Buchter *et al.* 2005 a & b). In addition, the available information is difficult to interpret and occasionally even contradictory. For example, Nkenke *et al.* (2002) used a rabbit model to compare the osteotome technique with the conventional drilling technique. They showed that, eight-weeks after implant placement, the bone-to-implant contact ratio was not significantly different for the osteotome technique compared to the conventional implant placement. However, it has to be noticed that no mechanical data were provided about the final fixation of the implants in the bone.

On the other hand, human clinical studies dealing with the osteotome technique suggest that a 100% success rate can always be achieved after implant loading (Komarnyckyj 1998; Fugazzotto 2002; Rodoni 2005), but the osteotome approach is mostly used for sinus elevation procedures in these studies rather than for implant socket preparation.

Besides the use of the osteotome technique and the resulting osteocompression to achieve high initial implant stability, so-called "undersized drilling" can be used to create a wanted level of implant stability. The amount of required misfit between implant diameter and drill hole is determined by the bone density of the implant recipient site (Skalak & Zhao 2000a). This effect of drill hole diameter can be further affected by the shape and height of the implant surface roughness (Skalak & Zhao 2000a). In view of this in the current study, the effect of surgical technique as well as implant surface roughness on final implant fixation were evaluated by mechanical testing of the implant and scanning electronic microscopic (SEM) evaluation of the bone-to-implant interface response after 12 weeks of healing.

Materials and methods

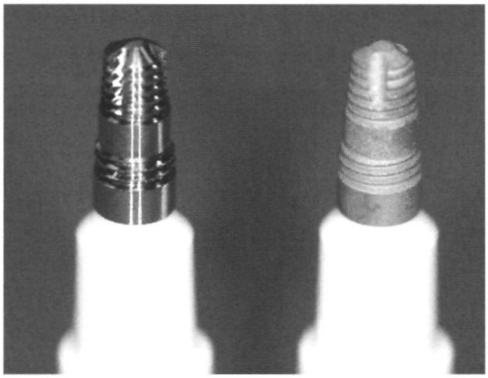
Implant

Fourty-eight conically shaped, screw-designed oral implants (Biocomp® Industries, Vught, The Netherlands) were used (Figure 1). All implants were made of commercially pure titanium, measured 10 mm in length, and had a diameter of 4.6 mm.

The implants were divided into two groups according to surface topography: turned (machined) group and grit-blasted and acid-etched (roughened) group.

Universal Surface Tester (UST®, Wurzburg, Germany) was used to characterize the different surface topographies. The equipment included a diamond stylus, consisting of a 60° cone, which was moved across a surface wit h a load of 10 Nm. Three screws of each surface type were selected at random and measured.

Figure 1 Machined and etched implants as used in the study.



Animal model and implantation procedure

Eight healthy mature female Saanen goats, 2-4 years of age and weighing about 60 kg, were used in this study. Before surgery, blood samples of the goats were taken to ensure that the animals were free of Caprine Arthritis-Encephalitis (CAE/CL). The animals were housed in a stable. National guidelines for the care and use of laboratory animals were observed.

General anesthesia was induced by an intravenous injection of pentobarbital and maintained by ethrane 2-3% through a constant volume ventilator administered through an endo-tracheal tube. The goats were connected to a heart monitor. To reduce the risk of peri-operative infection, the goats were treated according to the following doses of antibiotics: during the operation: Ampicillin (Albipen®, Intervet BV, Boxmeer, The Netherlands) 15 %, 3 ml/50 kg s.c., one and three day after the operation: Ampicillin (Albipen® LA, Intervet BV, Boxmeer, The Netherlands), 7.5 ml/50 kg s.c..

To place the implants into the trabecular bone of the femoral condyles, the animals were immobilized on their backs and the hind limbs were shaved, washed and disinfected with povidone-iodine. A longitudinal incision was made on the medial surface of the left and right femurs and the femoral condyles were exposed. Three holes were drilled in each femoral condyle at least 1 cm apart. The bone preparations were performed with a gentle surgical technique, using low rotational drill speeds (max. 800 rpm) and continuous internal cooling. After preparation the holes were irrigated and then packed with sterile cotton gauze to stop bleeding Each femoral condyle had three implant sites, resulting in six implants in each goat

For the installation of the femoral implants, three different surgical approaches were used

- ❖ Approach 1 – Press-Fit Technique After exposure of the condyle, a hole was drilled with a consecutive series of drills to a final diameter of 4 6 mm
- ❖ Approach 2 - Undersized Preparation Technique The final drill as used in the procedure had a diameter of 4 mm
- ❖ Approach 3 – Osteotome Technique A pilot hole was prepared with a drill of 2 55 mm in diameter A series of consecutive osteotomes (spreaders) were then used to enlarge the diameter of the pilot hole to a diameter of 4 6 mm (osteotome diameters were 3 4, 4 0, and 4 6 mm) Each osteotome or spreader was left in place for one minute

All implants were manually placed, however, in six goats a Digital® torque instrument (MARK-10 Corporation, New York, USA) was used to measure the insertion torque value No significant differences in insertion torque were observed between the different implant surfaces and surgical techniques After placement of the implants, the soft tissues were closed in separate layers using resorbable vicryl 3-0 sutures Evaluation of the bone fixation was planned at an implantation period of 12 weeks At the end of the implantation period the goats were killed by an overdose of Pentobarbital (Nembutal® Apharmo, Arnhem, The Netherlands) and the implants with surrounding tissue were retrieved for mechanical and scanning electron microscope (SEM) evaluation

Mechanical testing and interface evaluation

For the mechanical testing, the goat condyles (8 condyles, 48 implants) were retrieved and the specimens were stored on ice at a temperature of approximately 4° C After arrival at the laboratory, implant fixation was measured using a torque removal test The torque-measurement device detected and registered the torque necessary to remove the implant The specimens were embedded in a mold with gypsum and placed on a support jig that was adaptable in multiple directions to ensure that a longitudinal force was placed on the implant. A tensile bench was used to slowly and gradually apply increasing torque (displacement 0 5 mm/min) to each implant until it loosened When the peak force representing implant loosening was reached, the torque-out procedure was finished

Following the mechanical testing, the torqued specimens were divided in smaller samples containing one implant each These samples were embedded in methylmetacrylate (MMA) After polymerization, the specimens were hemi-sectioned perpendicularly along the longitudinal axis of the implants with a diamond blade sawing machine Subsequently, the implant containing surface of these specimens were polished, ultrasonically cleaned with 100% aethylalcohol for 5 min and carbon coated for evaluation of bone-implant interface by SEM (JEOL 6310, Jeol Ltd , Tokyo, Japan) to determine the bone-implant response as well as where the interface failure during the torque test had occurred

Statistical analysis

Mean values and standard deviations (SD) were calculated One-way analysis of Variance (ANOVA) with a Tukey test was used for comparing the differences between groups Differences were considered as significant when $p < 0\ 05$ All calculations were performed using GraphPad® Intant 3 05 software (GraphPad Software Inc, San Diego, CA, USA)

Results

Surface topography characterization

Surface topographic evaluation demonstrated that both experimental surfaces differed in surface roughness (Table 1) The machined surface showed an average surface roughness value (R_a = 0 45 µm) that was significantly lower than that of the etched surface (R_a = 1 47 µm) The values for the parameter R_{sk} (Table 1) showed that the two surfaces had a positively skewed surface, the surfaces consisted of more peaks than valleys Although the data appeared to indicate that the etched implants had a higher R_{sk} mean value, statistical testing revealed that the difference was not significant (Table 1)

Experimental animals

Throughout the experimental period, the test animals appeared to remain in good health At sacrifice, no clinical signs of peri-implant inflammation or adverse reactions were clinically observed

Mechanical testing

The results of the torque measurements are listed in Table 2 and depicted in Figure 2. The highest mean removal torque value (98.5 ± 28.5 Ncm) was observed for the etched implants installed with the under-sized approach. Nevertheless, statistical testing showed that a significant difference existed only between etched implants placed using the under-sized approach compared to machined implants placed using the osteotome approach (Table 2).

Table 1 The mean ± SD value of surface roughness parameters

	Machined	**Etched**	***p* value**
R_a	0.45 ± 0.32	1.47 ± 0.54	$p < 0.05$
R_q	0.29 ± 0.1	1.82 ± 0.68	$p < 0.01$
R_{sk}	0.08 ± 0.35	0.29 ± 0.35	$p > 0.05$

Amplitude parameters (Wennerberg)

$\mathbf{R_a}$ – the arithmetic mean of the absolute values of the surface departures from a mean plane within the sampling area. It is measured in micrometers.

$\mathbf{R_q}$ – the root mean square value of the surface departures within the sample area. It has the statistical signification as the standard deviation of the height distribution.

$\mathbf{R_{sk}}$ – the measure of the symmetry of surface deviations about the mean plane. A negatively skewed surface has more valleys than peaks.

SEM evaluation

In general, all implants showed new bone formation and interfacial bone contact. Implants with high failure values showed a lot of bone formation and a good interfacial bone contact (Figure 3). On the other hand, all implants with a low failure value showed the presence of fibrous tissue over a considerable length of the implant surface (Figures 4).

The torque test resulted in a fracture at the bone-implant interface. Fracture was especially observed in the area where close bone-implant contact was achieved (Figure 5).

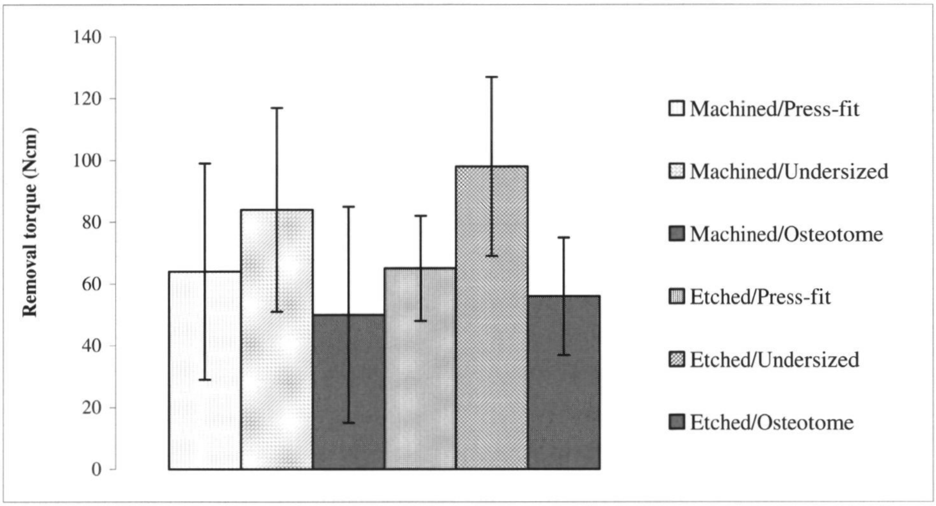
Table 2 The mean ± SD (Ncm) of the insertion (n=6) and removal torque (n=8) values.

Group	Placement technique	Torque test	Mean ± SD
Machined	Press-fit	Insertion	88 ± 45
Machined	**Press-fit**	**Removal**	**64 ± 35**
Machined	Undersized	Insertion	86 ± 42
Machined	**Undersized**	**Removal**	**84 ± 33**
Machined	Osteotome	Insertion	81 ± 18
Machined	**Osteotome**	**Removal**	**50 ± 35**
Etched	Press-fit	Insertion	71 ± 29
Etched	**Press-fit**	**Removal**	**65 ± 17**
Etched	Undersized	Insertion	85 ± 39
Etched	**Undersized**	**Removal**	**98 ± 29**
Etched	Osteotome	Insertion	72± 17
Etched	**Osteotome**	**Removal**	**56 ± 19**

Machined osteotome removal torque compared to Etched undersized removal torque= $P<0.05$.

Machined implants showed the presence of more bone between screw threads in the coronal portion of the implant compared to the apical part. In this area, the implants were partly lined with soft tissue consisting of fibrous connective tissue. In the area where the bone was in close contact with the implant surface, bone tended to grow down to the bottom of the threads (Figure 6). In approach 1, trabecular bone was seen to be in contact with tips of the screw threads. In approach 2, the amount of bone implant contact was less prominent compared to etched implants. In approach 3, a considerable area of the implant surface showed fibrous tissue formation.

Figure 2 Graph showing the removal torque values (mean ± SD) obtained with the various approaches.



Etched implants appeared to support more bone growth compared with the machined implants. Bone was in contact with the entire implant surface, including the inner diameter of the screw threads. Frequently, all screw tips were in contact with bone tissue (Figure 7 & 8). In approach 2, most screw threads were filled with bone tissue; both along the superior and inferior flank as well as the root area of the screw thread.

Figure 3 Backscatter SEM micrographs of an etched implant placed using an undersized approach. (A) Overview at magnification x25. Note the intimate apposition of bone trabeculae to the implant surface. (B) Higher magnification (x 150) of the threaded area. The fracture caused by mechanical testing occurred at the implant-bone interface (black line). Bone can be seen in close apposition to the implant surface. (C) Higher magnification (x 400) of the flat implant part. Again the fracture line induced by the torque testing can be clearly recognized. Also, at the flat implant part a tight implant-bone contact existed.

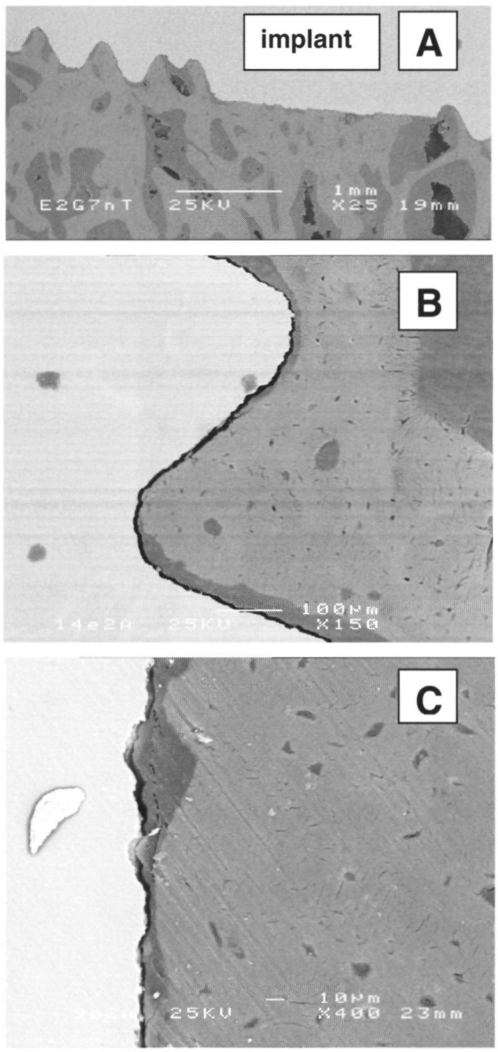


Figure 4 Backscatter SEM micrograph of a machined implant placed by the osteotome approach (original magnification x 25). Bone is growing into the screw-threads and is in close contact with the flat implant part.

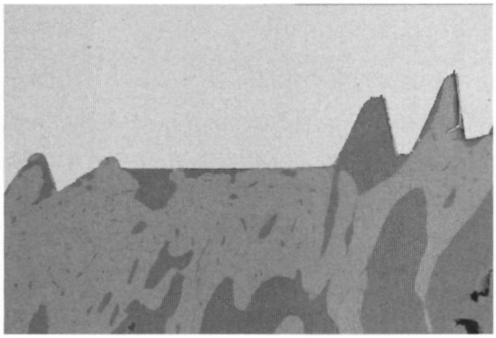


Figure 5 Backscatter SEM micrograph of machined implant placed by the press-fit technique showing a fracture line at the implant interface as a consequence of the removal torque test (original magnification x 500). The occurrence of the interfacial failure confirms the rigid implant-bone fixation.

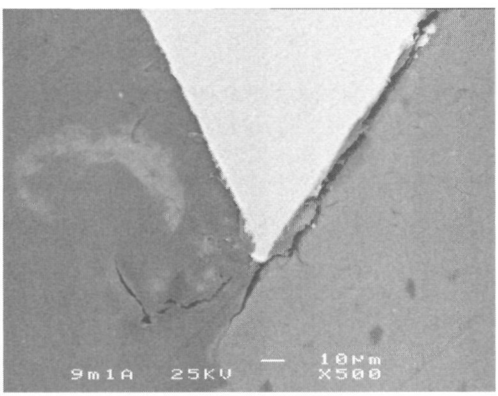


Figure 6 Backscatter SEM micrograph of a machined implant placed by the press-fit method (original magnification x 15). The trabecular nature of the bone surrounding the implant can be observed. Bone tissue has grown in the majority of the screw-threads. The amount of bone contact at the flat implant part is very limited.

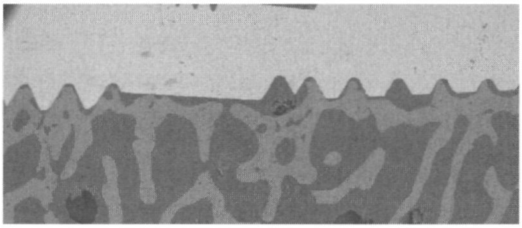


Figure 7 Backscatter SEM micrograph showing the threaded part of an etched implant placed by the press-fit technique (original magnification x 75). Again the fracture line caused by mechanical testing can be recognized at the implant interface. There is bone-to-implant contact with one of the screw-threads (right hand bottom corner), while no bone contact is present with the other screw-threads.

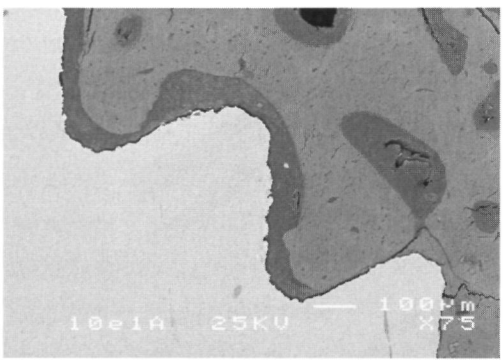
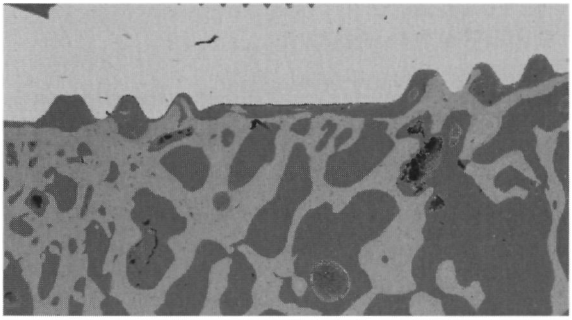


Figure 8 Backscatter SEM micrograph of an etched implant placed by the osteotome approach (original magnification x15). The bone that surrounds the implant has trabecular morphology. The amount of bone contact is very limited and occurs with only a few tips of the screw-threads.



Discussion

The aim of this study was to investigate the effect of surface roughness and different surgical techniques on the mechanical fixation of titanium oral implants 12 weeks after installation.

The main finding of this in vivo study using the goat model was that the etched implants placed with an undersized approach showed the highest removal torque values.

To obtain information about the bone-implant interface strength, mechanical evaluation of retrieved implants must be performed. For threaded implants, the most appropriate choice is the use of torque testing. In addition, a thorough analysis of the fractured interface is necessary after the torque testing to determine whether the torque failure is indeed caused by failure of the bone-implant interface. Reverse torque testing primarily places shear forces on the root-form implant around its cross section, although it is important to keep in mind that this method of loading may not directly relate to long-term clinical application (Jividen & Misch 2000).

Comparable other studies have been performed by such researchers as Buchter *et al.*, who placed implants with surfaces that were sandblasted with large grit and acid-etched (ITI SLA, Straumann GmbH, Freiburg, Germany) in the tibial metaphysis of minipigs. They compared osteotome preparation with an undersized preparation technique in which there was a discrepancy of 0 6 mm between the last drill and implant diameter *i.e.* the last spiral drill was 3.5 mm in diameter and the implant was 4 1 mm in diameter. After a healing period of 28 days, removal torques values were 111 5 and 59 Ncm for undersized and osteotome techniques, respectively Their reported results were comparable to the etched undersized and osteotome preparation groups in the present study

However, it has to be noticed that most of the reported studies showed a wide variation in their respective used animal models as well as implant location (Gotfredsen *et al.* 1992; Bumgardner *et al.* 2000, Klokkevold *et al* 2001; Steigenga *et al.* 2004; Sul 2004). Further, it is known that local bone conditions (quantity and quality) vary significantly between various animal species (An & Friedman 1999) Therefore, comparison and extrapolation of data with other studies is complex and can result in misinterpretation As a consequence, bonding strength data are only true for a specific experiment performed under strictly specific conditions.

Basically, the difference between the undersized and osteotome technique is the degree of bone compression. Both approaches result in bone compression around the implant, but in the osteotome technique the compression is clearly higher because of force-fitting stresses (Skalak & Zhao 2000a), which arise when an implant is placed into an implant bed of smaller diameter. They showed that substantial stresses can be generated even when the diameter of the implant is only 100 microns smaller than the hole in the bone (Skalak & Zhao 2000a). In view of this, the current failure of the osteotome technique to show the best result can be attributed to the high stress on the bone surrounding the implant bed in combination with the relatively high density of the trabecular bone of the femoral condyles. It has to be emphasized that the osteotome technique is designed to be used in Type-4 bone (Lekholm & Zarb 1985), while the density of condylar trabecular bone is somewhat higher. Unfortunately, no appropriate implant locations are available in large animals that both meet this bone type requirement and provide adequate available bone for the installation of implants. Furthermore, it cannot be excluded that a 3-month healing time is already too long because it results in remodelling of the newly formed bone tissue and a decrease in bone volume (Cardaropoli *et al* 2003)

In view of the present findings, some commentary is warranted on the final biological effect of implant surface morphology. Abrahamsson *et al.* (2004) showed similar characteristics with resorptive and appositional events for both grit-blasted and acid-etched (SLA) and turned surfaces, but the rate and degree of osseointegration were superior for the SLA compared with the turned implant surfaces Rota & Beloti (2003) suggested that, for titanium implants, Ra values ranging from 0.80 to 1.90 micrometers optimized both intermediary and final cellular responses, but did not affect the initial response, while smoother surfaces did not favor the cellular response at all. It has been implied that surface roughness changes the type and amount of protein adsorbed to the implanted material (Deligianni *et al.* 2001). Further, surface roughness may also influence cell spreading. Some researchers have theorized that, on rough materials, cells form attachment sites on different peaks of the implanted material In contrast, cells on a smooth material will form all their attachment sites in one plane, on the ventral side of the cells resulting in larger lateral spreading[33]. Attachment sites are linked to the cytoskeleton, which is involved in the generation of mechanical tension within the cell (Ter Brugge *et al.* 2002) The degree of spreading may influence the amount of force generated within the cells, which may directly influence biochemical signals in the cell (Chicurel *et al* 1998; Galbraith & Sheetz 1998) In this way, surface roughness may directly influence the phenotype and gene expression of cells on a titanium surface (Kim *et al.* 2005). Increase of the size of the blasting particles to 300 micrometers does not further enhance the initial attachment of bone cells compared to turned surfaces and those blasted with 63- to 90-micrometer particles (Mustafa *et al.* 2001) Similar to these bone cell studies, implants with an average surface roughness of 0 9-1.3microns were found to be optimal for bone fixation in a rabbit bone model for 12 weeks healing (Wennerberg *et al.* 1995)

Finally, a comparison has to be made between the current study and its predecessor in vitro study where similar implants and surgical techniques were used (Shalabi *et al.* 2006). This in vitro study showed that, directly after placement, not only the insertion and removal torque values for etched implants placed using an undersized technique was higher compared to machined implants, but that also the initial amount of bone-to-implant contact was higher for the etched implants Although a direct cellular effect of surface roughness cannot be excluded, this initial higher amount of bone contact can still be the reason for the higher removal torque of the etched implants from undersized sites in the present in vivo study. In view of this, a thorough histological and histomorphometrical assessment has to be performed to determine the amount of bone contact 12 weeks after placement of the implants

Conclusions

Supported by the mechanical failure data, it was concluded that etched implants placed using an undersized approach resulted in superior bonding strength with the surrounding bone and appear to improve the early fixation of oral implants in the femoral condyle of the goat

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Chapter 6

A histological evaluation of implants placed with different surgical technique into the trabecular bone of goats

Abstract

Objective: The aim of this study was to investigate the influence of implant surface topography and surgical technique on bone response

Materials and Methods: For the experiment 48 screw designed implants were used with two different surface finishes, i.e · machined and "blasted, etched". The implants were inserted in the left and right medial femoral condyle of 8 goats using three different surgical approaches press-fit (implant diameter = implant bed diameter), undersized (implant bed diameter < implant diameter) and osteotome. Each femoral condyle received 3 implants After an implantation period of 12 weeks the implants were retrieved and prepared for histological and histomorphometrical evaluation (bone contact and bone mass).

Results: Light microscopy revealed that in general the bone response to all implants was very similar. On the other hand, histomorphometry suggested that the bone-to-implant contact for the "blasted, etched" implants inserted by an undersized technique was higher compared with machined implants and the other surgical approaches, but the observed differences were not significant. Bone mass measurements did not reveal the occurrence of clear differences between groups and surgical approaches

Conclusion: Supported by our findings, we conclude that implants provided with a "blasted, etched" surface and installed in trabecular bone using an undersized preparation technique appear to support an enhanced bone-implant contact The use of an osteotome technique did not lead to improved results

Introduction

An important factor to establish a strong bone-to-implant interface is the surgical technique as used for the installation of oral implants (Albrektsson *et al* 1981) Surgical trauma together with anatomical conditions is supposed to be the key etiological factor for early implant loss (Esposito *et al* 1998, a & b)

In view of the above mentioned, it is known that the clinical success rate of oral implants inserted in so-called Type 3 and 4 bone is less compared with implants installed in Type 1 and 2 bone Compromised initial implant stability in bone of low density can be a reason for this lower success rate A recently introduced solution for this problem is the use of an osteotome technique for the preparation of the implant bed The goal of this technique is to insert the implant with a high degree of stability without additional bone removal loss, which is theoretically believed to improve the final bone healing (Skalak and Zhao 2000, a & b) Human clinical studies showed already a 100% success rate of loaded implants using the osteotome technique (Summers 1994, Komarnyckyj & London 1998, Fugazzotto 2002) However, it has to be noticed that these favorable clinical data are not supported by results as obtained in experimental animal studies In contrast, the animal studies even contradict the human studies For example, Buchter *et al* demonstrated in a minipig animal model that after 7 days of implantation no significant difference existed in bone-to-implant-contact (BIC) ratio between screw-type implants inserted with the osteotome or conventional preparation technique After 28 days, the conventional installed implants became statistically significant better in BIC ratio In addition, the extent of direct bone/implant contact was enhanced in conventionally prepared implant sites (Buchter *et al* 2005) Also, Nkenke *et al* (2002) did an animal study to the effect of the osteotome technique They inserted titanium plasma-spray coated step-designed implants placed in the femoral condyle of rabbits At two and four weeks, BIC was significantly better for the osteotome technique However, after eight weeks the BIC ratio was no longer statistically significant between osteotome technique and conventional implant placement Besides, qualitative fluorescence microscopy showed an earlier and stronger signal for the osteotome technique than the control group An explanation for this discrepancy in clinical and animal results can be the used implant type, because it is known that the interfacial shear stress, i e the resistance to loading and initial fixation, is influenced by both implant design and implant surface characteristics, like the implant surface roughness

Consequently, the purpose of the present study was to evaluate histologically the bone response to implants provided with two different surface topographies and installed with three different surgical approaches

Materials and methods

Implant

Forty eight commercially available conically-shaped screw designed oral implants (Biocomp® Industries, Vught, The Netherlands) were used All implants were made of commercially pure titanium and measured 10 mm in length and had a diameter of 4 6 mm

The implants were divided into two groups with each a different surface topography, i e turned (machined) and roughened (by grit-blasting and additional acid etching)

A Universal Surface Tester (UST® Wurzburg, Germany) was used to characterize the different surface topographies UST equipment enables objective statements about e g 3D evaluation of material surface topography The UST unit allows characterization of flat as well as structured surfaces The equipment includes a diamond stylus, consisting of a 60° cone, which is moved across a surface with a load of 10Nm The traverse range in the x-direction is 50 mm and in the y-direction 25 mm Three screws of each surface modification group were selected at random and measured

Animal model and implantation procedure

Eight healthy mature (2-4 years of age) female Saanen goats, weighing about 60 kg were used in this study National guidelines for the care and use of laboratory animals were observed

The operation was performed under general anesthesia To reduce the risk of peri-operative infection, the goats were treated according to the following doses of antibiotics during the operation Albipen® (Intervet BV, Boxmeer, The Netherlands) 15 %, 3 ml/50 kg s c , one and three day after the operation Albipen® LA, 7 5 ml/50 kg s c

All implants were placed into the trabecular bone of the femoral condyles A longitudinal incision was made on the medial surface of the left and right femur and

the femoral condyles were exposed Subsequently, three holes were drilled in the femoral condyle The distance between the femoral holes was at least 1 cm The bone preparations were performed with a gentle surgical technique, using low rotational drill speeds (max 800 rpm) and continuous internal cooling Each femoral condyle had three implant sites, resulting in six implants in each goat
For the installation of the femoral implants three different surgical approaches were used

1 In approach 1, a press fit technique was followed After exposure of the condyle, a hole was drilled with a consecutive series of drills to a final diameter of 4 6 mm
2 In approach 2, an undersized preparation procedure was done The final drill as used in the procedure had a diameter of 4 mm
3 In approach 3, a pilot hole was drilled with a drill of 2 55 mm in diameter Then, a series of consecutive osteotomes (spreaders) were used to enlarge the diameter of the pilot hole to a diameter of 4 6 mm (osteotome diameters were 3 4, 4 0, and 4 6 mm) Each osteotome or spreader was left in place for one minute

All implants were inserted manually After placement of the implants, the soft tissues were closed Evaluation of the bone fixation was planned after an implantation period of 12 weeks At the end of the implantation period the goats were killed by an overdose of Nembutal® (Apharmo, Arnhem, The Netherlands)

Histological procedures

After sacrificing the animals, the femoral condyles were excised and excess tissue was removed Then, using a diamond saw, the retrieved condyles were divided in smaller specimens, suitable for histological processing Each specimen was containing one implant site with surrounding bone Subsequently, the specimens were fixed in formaldehyde 4%, dehydrated in ethanol and embedded in methylmethacrylate (MMA) After polymerization in MMA thin (10 μm) non-decalcified sections were prepared with a modified diamond blade sawing microtome technique These sections were made perpendicularly on the longitudinal axis of the implant The sections were stained with methylene blue/basic fuchsine and examined with a light microscope (Leica Qwin Pro, Wetzlar, Germany)

Histological and histomorphometical analysis

All sections were evaluated on basis of a thorough histological description and histomorphometrical measurements Bone contact percentages and amount of bone mass around the implant was quantified.

All quantitative measurements were performed for three randomly chosen sections of implant

The presented data are the average of three measurements.

A Percentage of bone implant contact

The amount of interfacial bone contact was measured starting at the top of the flat middle part of the implant till the last apical screw-thread. Measurements were done both at the right and left side of the implants (Figure 1)

B Bone mass around the implants

The bone mass in rectangular regions along the implant was determined. Three region of interest (ROI), i e. ROI 500, ROI 1000 and ROI 1500, were marked (Figure 1) Each ROI had a width of 0.5 mm and a length of 2 mm, resulting in total area of 1mm^2 The bone mass was quantified in µm^2 10^5

Statistical analysis

Mean values and standard deviation (SD) were calculated. One-way analysis of Variance (ANOVA) with a Tukey test was used for comparing the differences between groups. Differences were considered as significant when $p < 0\ 05$. All calculations were done with GraphPad® Intant 3 05 software (GraphPad Software Inc, San Diego, CA, USA)

Results

Surface topography characterization

Surface topographic evaluation demonstrated that both experimental surfaces differed in surface roughness (Table 1). The machined surface showed an average surface roughness (R_a = 0 45 µm), which was significantly lower than the "blasted, etched" surface (R_a = 1.47 µm) The values for the parameter R_{sk} showed that the two surfaces had a positively skewed surface; the surfaces consisted of more peaks than valleys. Although, the data appeared to indicate that the "blasted, etched" implants had a higher R_{sk} mean value, statistical testing revealed that the difference was not significant (Table 1)

Figure 1 The implant with indication of the histomorphometrical evaluation parameters: (A) % bone contact; (B) amount of bone in three regions of interest (ROI), ROI 500 (1), ROI 1000 (2) and ROI 1500 (3).

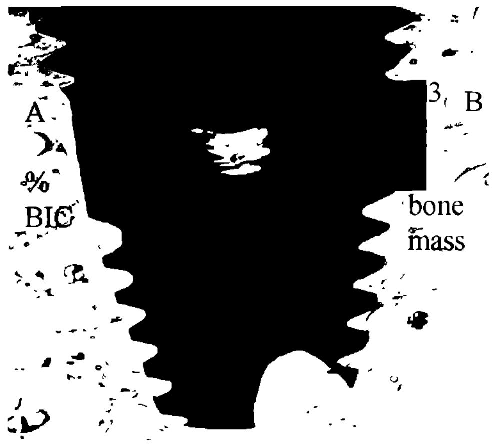

Table 1 The mean ± SD value of surface roughness parameters

	Machined	"Blasted, etched"	*p* value
R_a	0.45 ± 0.32	1.47 ± 0.54	$p < 0.05$
R_q	0.29 ± 0.1	1.82 ± 0.68	$p < 0.01$
R_{sk}	0.08 ± 0.35	0.29 ± 0.35	$p > 0.05$

Amplitude parameters (Wennerberg)

R_a – the arithmetic mean of the absolute values of the surface departures from a mean plane within the sampling area. It is measured in micrometers.

R_q – the root mean square value of the surface departures within the sample area. It has the statistical signification as the standard deviation of the height distribution.

R_{sk} – the measure of the symmetry of surface deviations about the mean plane. A negatively skewed surface has more valleys than peaks.

Experimental animals

Durıng the experımental perıods, two goats had to be sacrıfıced one due to broken leg and the other goat maıntaıned dıffıculty ın walkıng after surgery The rest of the anımals remaıned ın good health As a consequence, 36 ımplants (n = 6 for each ımplant type and surgıcal approach) were used for the hıstologıcal and hıstomorphometrıcal evaluatıon No clınıcal sıgns of ınflammatıon or adverse tıssue reactıon were observed around the remaınıng ımplants

Histology

The lıght mıcroscopıcal evaluatıon of the ımplants showed generally an uneventful healıng of all ımplants There were no sıgns of ınflammatıon All ımplants were ınserted for theır majjor part ın trabecular bone Regularly, contact could be observed between new-formed bone and the ımplant surface Frequently, also some ınterveníng fıbrous or marrow tıssue was present at the ınterface

“Blasted, etched” implants, press-fit technique: An ıntımate contact between the ımplant and surroundıng cortıcal and trabecular bone could be observed In the area, dırectly adjacent to the ımplant, new bone formatıon had occurred on the ımplant surface wıthout any ınterveníng soft tıssue layer In thıs area, also remodelıng lacunes wıth osteoblasts were vısıble Next to the ımplant, no accumulatıons of ınflammatory cells were seen At the cortıcal sıde, the screw threads were almost completely fılled wıth dense bone New bone formatıon was also observed at the apıcal part of the ımplants Most of the screw-threads were completely covered wıth bone Thıs bone was ın close contact wıth the ımplant surface wıthout any sıgn of fıbrous tıssue formatıon or ınflammatory reactıon (Fıgure 2)

“Blasted, etched” implants, undersized technique: Bone appositıon and bone remodelıng lacunae wıth marrow cells ın contact wıth the ımplant surface could be observed Ingrowth of newly formed lamellar bone ınto the screw threads was also observed However, ın contrast wıth etched ımplants ınserted accordıng the press-fıt technıque, the ıngrowth of the bone appeared to be more proceeded (Fıgure 3)

“Blasted, etched” implants, osteotome technique: The healıng process of both cortıcal and trabecular bone was almost ıdentıcal to the etched ımplants ınserted wıth the press fıt technıque Agaın trabecular bone ıngrowth ınto the screw threads seemed to be less abundant compared wıth etched ımplants ınserted by under-sızed or press-fıt technıque

Machined implants, press-fit technique: Frequently, the bone contact was still limited to the top of the screw threads On the other hand, the sections revealed clearly that the regeneration of bone started from the top of the screw thread and was conducted from this point over the implant surface into the screw thread

Machined implants, undersized technique: The cortical bone response was very similar to the undersized inserted, etched implants However, the trabecular bone ingrowth into the screw threads of this implants appeared to be less pronounced than for etched implants inserted with the undersized technique (Figure 4)

Machined implants, osteotome technique: These implants showed at the cortical side a similar bone formation compared with etched "undersized" implants Further, in the trabecular bone compartment, also abundant dense mature bone was closely laid down to the implant surface without intervening fibrous tissue interface (Figure 5)

Histomorphometrical evaluation

Percentage of bone contact

All the bone apposition data for the various implant surfaces are given in Table 2 Although the data suggested that the "blasted, etched" implants inserted by the undersized approach showed a higher bone contact percentage than the other groups, statistical testing of the findings using an one-way analysis of variance (ANOVA) and a Tukey multiple comparison procedure revealed that no significant differences ($P < 0\ 05$) in bone contact existed between the various surgical techniques and different surfaces

Bone amount

The results regarding the bone amount measurements are given in Table 3 Statistical testing (analysis of variance and Tukey multiple comparison) was focused on the possible existence of a difference in amount of bone mass between the different implant and surgical approaches The analysis revealed that no statistical significant differences existed between the various groups ($P < 0\ 05$)

Figure 2 Light photograph of an **"blasted, etched", press-fit implant**. Bone ingrowth into the screw threads can be observed. In between, bone contact sites alternating fibrous tissue as well as remodelling lacunes can be recognized. Original magnification x 10, bar = 100μm.

Figure 3 Light micrograph of an **"blasted, etched" undersized implant**. Close bone contact can be observed for this type of implant both around the threaded and flat part of the implant. (A) Original magnification x 10, bar = 100μm; (B) x 10, bar = 100μm.

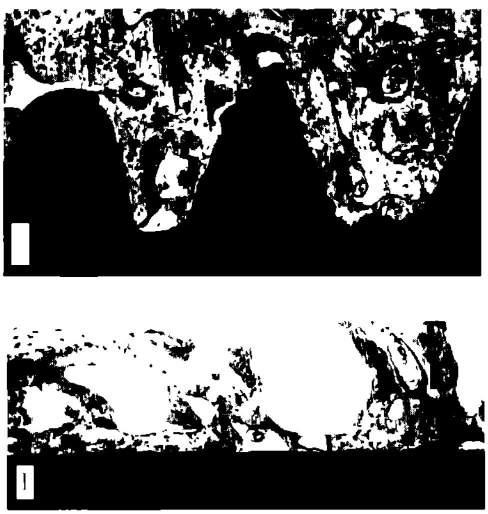

Figure 4 Light microscopical section of a **machined, undersized implant**, demonstrating bone deposition on the flat as well as threaded implant surface (A) Original magnification x 2 5, bar = 400μm, (B) x 10, bar = 100μm

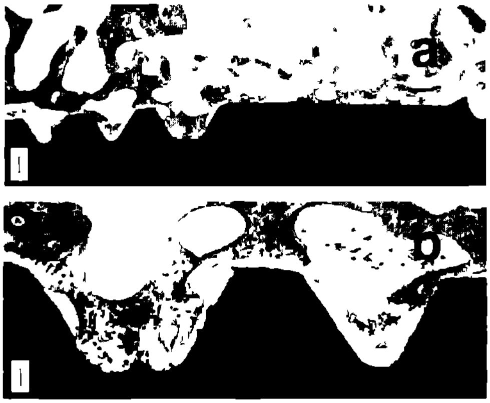

Figure 5 Histological picture of a **machined, osteotome implant** The bone around the implant shows a trabecular structure The screw threads at the cortical level are almost completely filled with dense bone Original magnification x 1 6, bar = 625μm

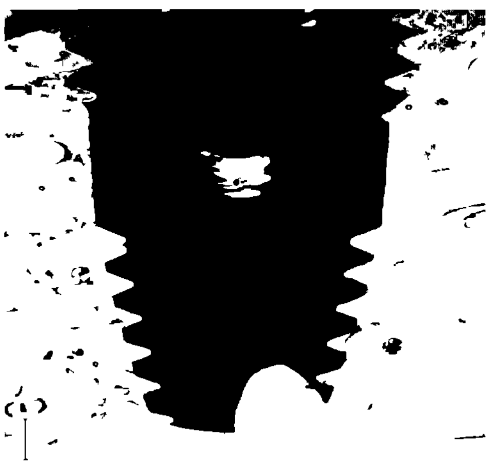

Table 2 Bone-implant contact percentages as measured along the flat surface and apical threads on the left and the right side of the implant.

Implant/technique	**Mean % bone contact ± SD**
Machined/press-fit	20 ± 11
Machined/under-size	24 ± 11
Machined/osteotome	30 ± 13
"Blasted, etched"/press-fit	28 ± 12
"Blasted, etched"/under-size	38 ± 9
"Blasted, etched"/osteotome	22 ± 8

Table 3 Measured amount of bone in $\mu m^2.10^5 \pm$ SD.

Implant/technnique	**ROI 500**	**ROI 1000**	**ROI 1500**
Machined/press-fit	5 ± 1	4 ± 1	4 ± 1
Machined/undersized	6 ± 1	5 ± 1	4 ± 1
Machined/osteotome	5 ± 1	5 ± 1	5 ± 1
"Blasted, etched"/press-fit	5 ± 1	6 ± 2	5 ± 1
"Blasted, etched"/undersized	5 ± 1	6 ± 2	5 ± 1
"Blasted, etched"/osteotome	5 ± 1	5 ± 2	5 ± 2

Discussion

The aim of the present study was to investigate the combined effect of implant surface roughness and surgical technique on bone healing.

Evaluation of our histomorphometrical data suggests that "blasted, etched" implants inserted by an undersized approach show increased bone implant contact compared with the other implants Unfortunately, statistical testing revealed that no significant differences in bone implant contact and bone mass existed between the various experimental groups Nevertheless, the tendency as observed corroborates with two of our earlier performed studies Firstly, in an in vitro study (Shalabi *et al*, 2006a) "blasted, etched" implants inserted by the undersized technique required the highest removal torque value to unscrew the implants directly after their installation Secondly, in a similar designed study as the present study, the mechanical fixation of the implants was tested by torque testing after 12 weeks of implantation (Shalabi *et al*, 2006b) Comparison of the obtained results shows that the highest removal torque values were obtained for "blasted, etched" undersized inserted implants which show now the best bone response

Basically, the difference between the undersized and osteotome technique is the degree of bone compression Although, both methods result in bone compression around the implant, the compression with the osteotome technique is higher because of force-fitting stresses, which arise when an implant is placed into an implant bed of smaller diameter (Skalak and Zarb 2000a) It has to be noticed that substantial stresses can already be generated when the diameter of the implant is only 100 microns smaller than the hole in the bone The current failure of the osteotome technique to show the best result can be attributed to a higher stress on the bone surrounding the implant bed in combination with the relatively high density of the trabecular bone of the femoral condyles compared with the undersized installed implants This explains also the discrepancy between clinical and experimental results, since there is a clear difference in density between animal and human bone

Further, our results are in agreement with other animal studies, which also evaluated bone healing around different implant surfaces For example, Grizon *et al* (2002) inserted implants with a rough and smooth surface in the femoral bone of sheep At 3 and 6 months after implantation, no difference in bone contact and bone volume was observed between the two types of implants, while at 12 and 18 months only a tendency existed for higher values around the rough implants Also, Gotfredsen *et al* (1992) found no significant difference in direct bone-to-implant contact between TiO_2-blasted implants and machined implants They installed the implants immediately in extraction sockets in the mandible of dogs and left them in place for 12 weeks Despite the lack of increased bone contact, the TiO_2-blasted implants required a higher removal torque to be unscrewed out of the bone

In contrast, it has to be noticed that there are also several investigators who demonstrated that variation in implant surface roughness results in both a different histological and mechanical bone response, like Novaes *et al* (2002) who compared 4 different types of implant surfaces, smooth (machined), titanium plasma spray coated (TPS), hydroxyapatite coated (HA), and sandblasted with soluble particles (SBM) The SBM-treated surface provided a significantly greater bone-implant contact than a machined surface after 90 days of implantation Also, Wennerberg *et al* (1997) found in rabbit model that one year after installation screw shaped rough implants had a significant firmer bone fixation and percentage of bone-to-implant contact than the machined implants In another study, this effect of surface roughness was observed to occur already after 12 weeks of implantation (Wennerberg *et al* 1996)

In view of the above mentioned, some comments have to be made about the used animal model The goat model for the evaluation of bone-implant behavior has already been used in our laboratory for about 16 years In the various studies a lot of different implant designs and implant materials (differing in surface chemical composition as well as surface microgeometry) have been tested A permanent parameter in the final histomorphometrical analysis of the bone-implant response was the bone-to-implant contact percentage Further, titanium implants with a similar roughness as used in the current study were included in all studies as reference material Surprisingly, comparison of the available "reference" data shows that the bone contact percentages differ significantly between the various separate studies and range from 15-57% An explanation for this observation, which is supported by the bone contact data of the present study, can be the used implant design as well as surgical technique The highest values were obtained with cylindrical- and screw-shaped implants inserted with an undersized approach, 57% and 49% respectively (Caulier *et al* 1995, Vercaigne *et al* 2000) and the lowest values with rectangular- and screw-shaped implants inserted in a press-fit approach, 15% and 22% respectively (Vercaigne *et al* 1998, Hulshoff *et al* 1997) In addition, it has to be noticed that (1) the implant design of the Hulshoff *et al* (1997) study was similar to the implant design as used in the current study, and (2) the bone contact data corroborate very well with those of the rough, press-fit inserted implants in the current study (22% vs 28%)

Finally, a remark has to be made about the lack of statistical significance Although, the data suggested that the etched, undersized installed implants performed better in terms of bone response, the observed difference was found to be not significant To determine statistical differences in biological performance, adequate observation periods and appropriate numbers of implant samples must be used Considering the observation time, we decided to evaluate the bone response after 12 weeks of implantation, because bone healing in goats is then completed For the calculation of the required sample size in an experiment, many formulas are presented in the literature (Pocock, 1983, Schlesselman, 1982) The choice for the best formula depends on both the chosen experimental design and the "measurement level" of the observations Important parameters in these formulas are (1) dispersion of the observations in any population of implant system (σ), and (2) threshold of relevance (δ) (Pocock 1983, Simes 1986) The choice for σ and δ is not simple in practice (Jansen and van't Hof, 1994) The value of σ has to be taken from the literature or from previous experiences in comparable experiments Previous studies learned that σ = 15-20% The value of δ cannot be assessed on statistical grounds, a pilot study to estimate δ is impossible "Relevance" is not dictated by outcome, but purely by the objectives of the experimental project Evidently, δ was not set appropriately resulting in insufficient power Nevertheless, it has to be emphasized that another order of magnitude for δ results in unrealistic group sizes of about 50-80 implants Consequently, the performance of experimental animal studies requires entering into a compromise taking into account that perhaps the combination of various animal studies (meta-analysis) can offer a solution

Conclusion

Supported by our findings, we conclude that implants provided with a "blasted, etched" surface and installed in trabecular bone using an undersized preparation technique appear to support an enhanced bone-implant contact The use of an osteotome technique did not lead to improved results

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Chapter 7

Bone response to titanium coated polymethyl methacrylate resin (PMMA) implants inserted into the tibia of goats

Abstract

Objective: The aim of the current study was to investigate bone behavior to titanium coated polymethylmethacrylate (PMMA) implants by micro-CT and histological evaluation

Materials and Methods: For the experiment titanium coated PMMA implants were used The implants had a machined threaded appearance and were provided with a 400-500 nm thick titanium coating The implants were inserted in the right or left tibia of 10 goats After an implantation period of 12 weeks the implants were retrieved and prepared for micro-computer tomography (µCT), light microscopy, and X-ray microanalysis

Results: The micro-CT showed that the screw-threads and typical implant configuration were well maintained through the installation procedure Overall, histological responses showed that the titanium-coated implants were well tolerated and caused no atypical tissue response In addition, the bone was seen in direct contact with the titanium-coated layer The X-ray microanalysis results confirmed the light microscopical data

Conclusion: In conclusion, the obtained results prove the final use of titanium-coated PMMA implants for evaluation of the bone-implant response using µCT However, this study also confirms that for a proper analysis of the bone-implant interface the additional use of microscopical techniques is still required

Introduction

A successful oral ımplant ıs characterızed by the occurrence of a dırect contact between the surroundıng bone and ımplant surface Qualıtatıve and quantıtatıve evaluatıon of the perı-ımplant tıssues around retrıeved ımplants ıs classıcally done by means of lıght mıcroscopy to confırm thıs requıred bone response Dıfferent technıques are avaılable to prepare hıstologıcal sectıons as well as dıfferent staınıng procedures can be used to obtaın ınformatıon about the specıfıc cellular and tıssue response However, a dısadvantage of hıstologıcal evaluatıon ıs that ıt provıdes only two-dımensıonal ınformatıon Hıgh-resolutıon three-dımensıonal data of confıguratıons wıth a multıfaceted structural desıgn, lıke oral ımplants, can be obtaıned by usıng mıcrofocus computer tomography (µCT) (Oosterwyck *et al* 2000) Analysıs of the bone response around tıtanıum ımplants by µCT has been found to be hıghly relıable for determınıng bone mass and bone densıty parameters For example, ın a recently publıshed study, 89% matchıng ın bone area measurements was observed comparıng µCT slıces wıth lıght mıcroscopıcal sectıons (Stoppıe *et al* 2005) On the other hand, metallıc ımplants cause so-called streakıng artıfacts due to scatterıng of X-rays, whıch prevents an accurate evaluatıon of the ınterfacıal bone-to-ımplant contact (Bernhardt et al 2004, Park et al 2005) Although, the placement of an alumınum fılter between detector and specımens can suppress thıs phenomenon, ıt cannot be completely avoıded (Stoppıe *et al* 2005) A better solutıon for thıs problem ıs the use of synchrotron radıatıon mıcrotomography (SRµCT) Due to the mıcroenergıtıc X-rays as used ın thıs technıques, scatterıng can be evaded, whıch results ın a hıgher sensıtıvıty of bone detectıon near the ımplant surface and allows the quantıfıcatıon of the dırect bone response (Bernhardt *et al* 2005) Unfortunately, SRµCT ıs not easy accessıble and the procedure ıs also very tıme consumıng

In vıew of the above mentıoned, ıt has been suggested that the use of thın tıtanıum coatıngs deposıted on polymerıc ımplants can offer an alternatıve optıon for analyzıng bone-ımplant contact usıng µCT-ımagıng (Stoppıe *et al* 2005) In the past, tıtanıum-coated polymerıc ımplants were already successfully used for transmıssıon electron mıcroscopıc analysıs of the cell and tıssue response (Albrektsson *et al* 1982 and Jansen *et al* 1985) and ultrastructural study of epıthelıal cell attachment to ımplant materıals (Jansen *et al* 1985 and Chehroudı *et al* 1991)

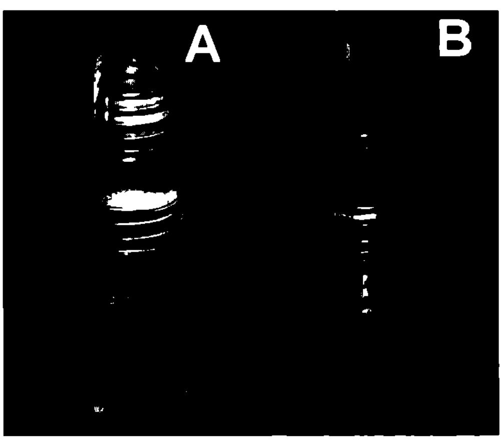
Consequently, the aim of the current study is to investigate the bone behavior by µCT and light microscopy using titanium-coated PMMA implants

Materials and methods

Implants

Ten conically-shaped screw designed PMMA implants were used All implants measured 10 mm in length and had a diameter of 4 6 mm The implants were copied and prepared with a lathe out of PMMA rod completely analog to metallic implants (Biocomp® Industries, Vught, The Netherlands) Subsequently, all ten implants were coated with a 400-500 nm thick layer of titanium (Ti) (Figure 1) The Ti layer was deposited using a radio frequency magnetron-sputtering unit (Edwards ESM 100) During the sputtering process, a commercially pure Ti target was used Pressure was kept at 5 0 $\times$ 10^{-3} mbar using argon gas, and the power level was set at 200 W The Ti target was sputter cleaned before deposition The target was considered clean when the plasma turned from pink to blue, resulting from blue light emitting Ti in the plasma The PMMA implants were sputtered for 30 min Finally, they were autoclaved for 15 min at a temperature of 121° C before use in the experimental animal study

Figure 1 Macroscopic pictures of a non-coated PMMA implant (A) titanium-coated PMMA implant (B) The titanium coating has a shiny, gray-black appearance



Animal model and implantation procedure

Ten healthy mature (2-4 years of age) female Saanen goats, weighing about 60 kg were used in this study Before surgery blood samples of the goats were taken to ensure that the animals were Caprine Arthritis-Encephalitis (CAE/CL) free The animals were housed in a stable National guidelines for the care and use of laboratory animals were observed

The operation was performed under general anesthesia and was induced by an intravenous injection of pentobarbital and maintained by ethrane 2-3% through a constant volume ventilator, administered through an endo-tracheal tube The goats were connected to a heart monitor To reduce the risk of peri-operative infection, the goats were treated according to the following doses of antibiotics during the operation Albipen® 15 %, 3 ml/50 kg s c , one and three day after the operation Albipen® LA, 7 5 ml/50 kg s c

All implants were placed into the tibia of the right or left hind limbs of the goats Therefore, the animals were immobilized on their back and the hind limbs were shaved, washed and disinfected with povidone-iodine Then, a longitudinal incision was made on the tibia of the left or right side and the bone were exposed Subsequently, a hole was drilled in the tibia with a consecutive series of drills to a final diameter of 4 6 mm The bone preparation was performed with a gentle surgical technique, using low rotational drill speeds (max 800 rpm) and continuous internal cooling After preparation, the hole was irrigated and then packed with sterile cotton gauze to stop bleeding Thereafter, the implant was inserted press-fit into the hole Only one implant was inserted in each goat

After placement of the implant, the soft tissues were closed in separate layers using resorbable Vicryl 3-0 sutures Evaluation of the bone fixation was planned at an implantation period of 12 weeks At the end of the implantation period the goats were killed by an overdose of Nembutal® and the implants with surrounding tissue retrieved for histological evaluation and µCT analysis

MicroCT evaluation

Implants were made of PMMA in order to allow the use of microCT Earlier studies have already shown that microCT cannot be used to evaluate the bone response in close proximity of full metallic or full ceramic implants Scattering occurs at the implant surface, which excludes proper evaluation This problem can be avoided by making use of polymeric implants (feasibility has been confirmed in previous studies) For microCT evaluation a 3D analysis of bone formation was done

After sacrificing the animals, the tibia including the implants were harvested immediately and fixed in formaldehyde 4% and dehydrated in ethanol Subsequently, the specimens were wrapped in Parafilm® to prevent drying during scanning and placed in the middle of a cylindrical sample holder Then, high-resolution scanning with a pixel size of 18 70 µm was performed at energy of 100kV and intensity of 98 µA (SkyScan-1072, Skyscan n v , Aartselaar, Belgium) Cone beam reconstruction (version 2 15, Skyscan®) was performed on the 452 projected files The number of cross-sections was set to cover the entire length of the implant The micro-CT 3D-Creator software was used to make a 3D-reconstruction from the obtained stack of reconstructed files

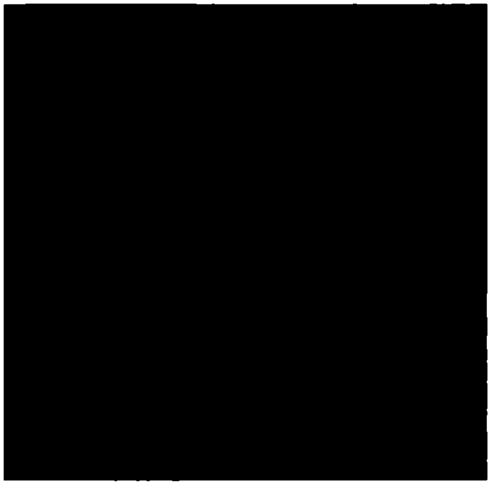
Histological procedures

Subsequent to µCT-scanning, the specimens were cut to smaller size suitable for histological processing Each specimen was containing one implant site with surrounding bone The specimens were then dehydrated in increasing ethanol concentrations and embedded (non-decalcified) in methyl methacrylate (MMA) for 4 weeks (Figure 2) After polymerization in MMA thin (10 µm) non-decalcified sections were prepared with a modified diamond blade sawing microtome technique These sections were made perpendicularly on the longitudinal axis of the implant The sections were stained with methylene blue/basic fuchsin and examined with a light microscope

X-ray microanalysis

Following histological sectioning, the surface of the remaining part of the tissue block was polished with 4000 grit silicon carbide sandpaper Subsequently, the blocks were cleaned with 70% alcohol and carbon coated Specimens were examined by scanning electron microscope (XL30 ESEM FEG, Philips, Eindhoven, the Netherlands) in backscatter mode at 20 kV, with an attached X-ray microanalysis system (EDAX with software, EDAX BV, Tilburg, the Netherlands)

Figure 2 Photograph of a tissue block after histological preparation, i.e. embedding in MMA. The implant part that has protruded in the medullar cavity is visible and confirms the maintenance of the coating during the installation process and 12 week implantation time.



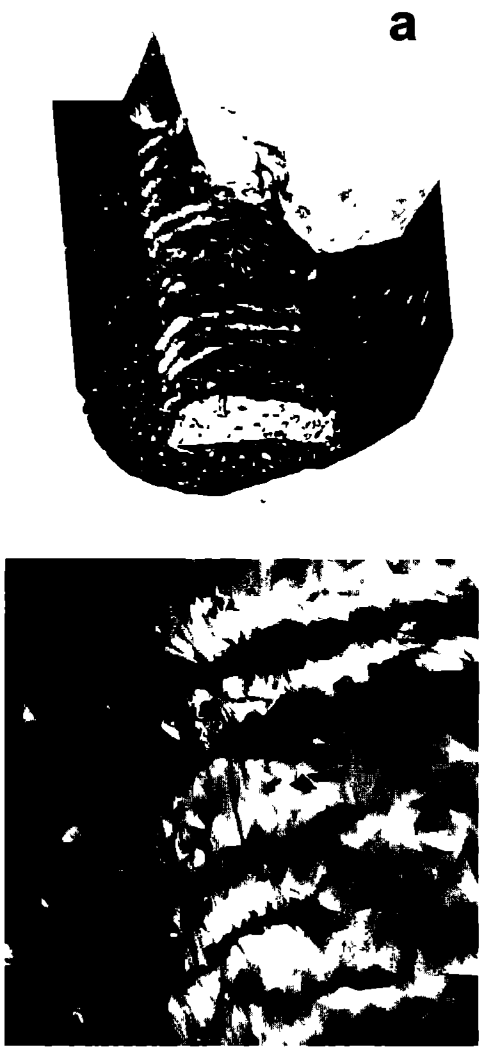
Results

During the experimental periods, all animals appeared to be in good health throughout the test periods. At sacrifice, no clinical signs of inflammation or adverse reaction were observed around the implants.

MicroCT evaluation

The 3-D reconstructed representations showed clearly the implants surrounded by cortical bone. Overall, the screw-threads and typical implant configuration were well maintained through the installation procedure. No streaking artifacts were present. The bone was found to be grown into the screw-threads and bone conduction into the marrow cavity was seen (Figure 3). Evidently, the titanium coating was not thick enough to allow visualization of the implant part that was positioned into the medullar cavity.

Figure 3 Micro-computer tomography pictures showing the bone appearance after installation of the PMMA coated implant by a press-fit approach. (A) The implant penetrated into the medullar cavity and ingrowth of bone at the endosteal side can be observed. (B) The screw-threads as well as the smooth implant surface can be recognized.



Histological description

A short embedding procedure prevented serious distortion of the bulk of the PMMA implants due to the required use of organic solvents.

The histological evaluation demonstrated that the titanium-coated implants were well tolerated by the tissues. In the cortical compartment of the tibia, bone was observed in close contact with the titanium layer, which could easily be recognized and appeared to cover the implant surface for almost 100% (Figure 4). The bone-titanium coating contact was almost continuous (Figure 5A) and only occasionally remodeling lacunas (Figure 5B) or an intervening fibrous tissue layer were seen. When fibrous tissue was present in the interface, this could frequently be associated with a lacking titanium coating (Figure 6). The bone around the implants showed a very organized structure in which osteons could be recognized. At the crestal side, the implants were always covered by newly deposited bone. At the apical side the implants penetrated

Figure 4 Histological picture of a titanium coated PMMA implant. The implant is surrounded by bone tissue in close contact with the titanium coating, which is visible as a thin black line of the outer surface of the implant. Magnification x1.6, bar= 625μm.

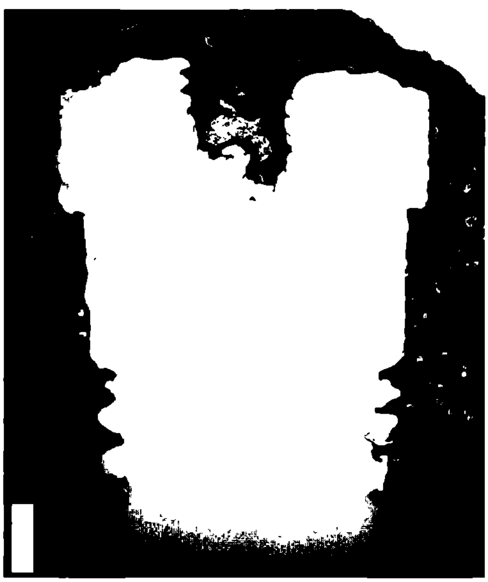


Figure 5 Histological section of titanium-coated implant showing clearly the titanium layer. (A) which was covered almost completely by bone, and (B) occasionally remodeling lacunas were present. Original magnification x10, bar= 100μm.

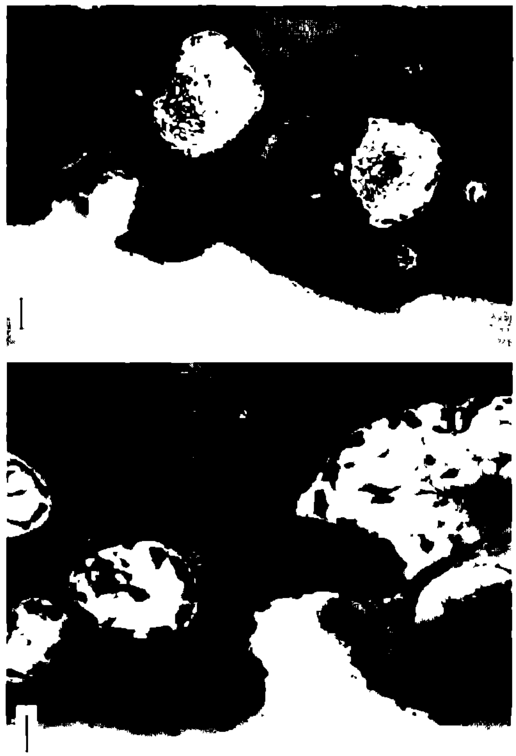
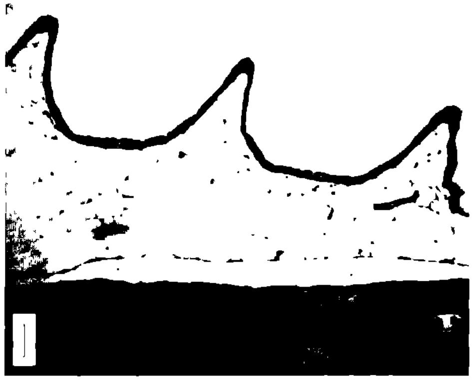


Figure 6 In areas where the coating was lacking, the implant surface was surrounded by fibrous tissue (black layer). Magnification x20, bar= 50μm.

Figure 7 The part of the implant that penetrated into the medullar cavity did not evoke any sign of an inflammatory response. Original magnification x10, bar= 100μm.

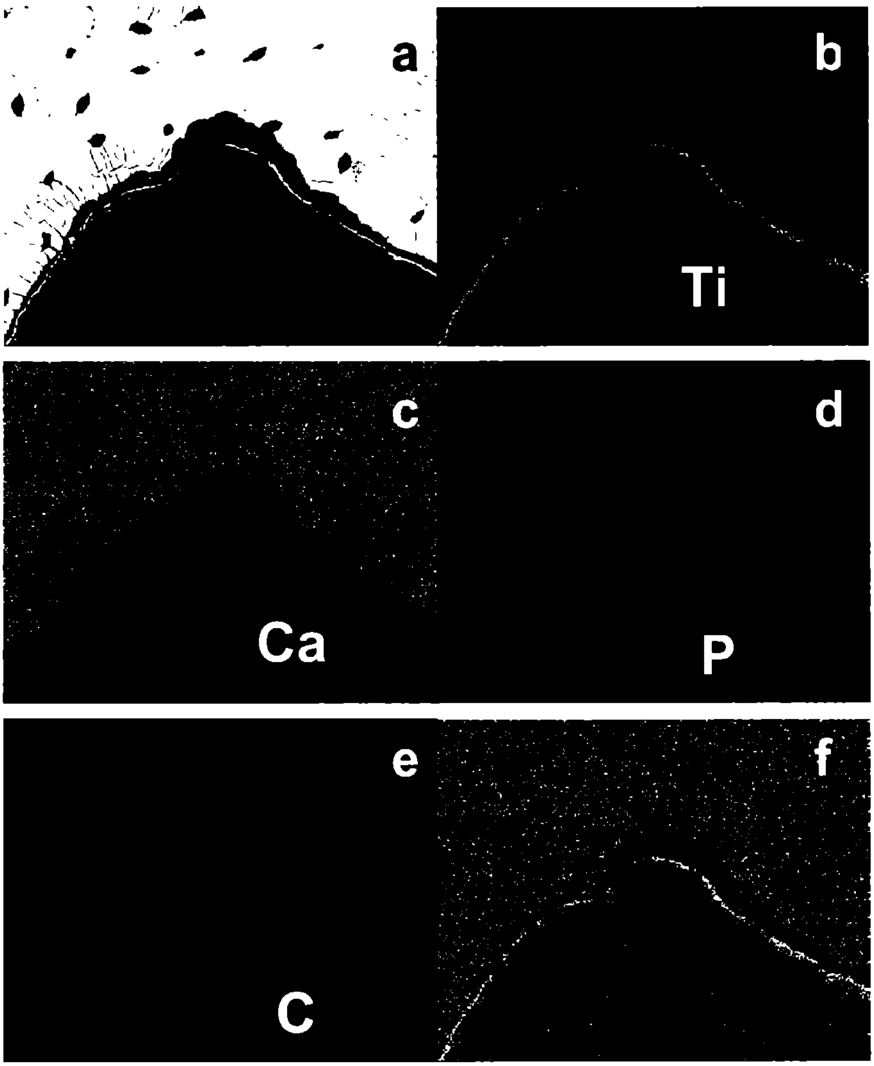


into the medullar cavity. Ingrowth of bone along the implant surface and into the medullar cavity had occurred. In the bone marrow, no sign of an inflammatory response indicating a foreign body reaction was seen (Figure 7).

X-ray microanalysis

Backscatter electron microscopy confirmed the light microscopical data. The PMMA material of the implant could be recognized as well as the titanium coating that covered the implant surface. Bone was seen in close contact with the major part of the implant surface. Figure 8A shows a cross-section where bone is not in direct contact with the titanium coating. Figures 8B-E_show a mapping of the PMMA implant-bone interface with regard to the presence of titanium, calcium, phosphorus, and carbon. The presence of calcium and phosphorus indicates the presence of bone and carbon indicates the coating as deposited onto the tissue block as required for backscatter electron microscopy. An integral mapping, as depicted in Figure 8F, verifies that a gap existed between implant and bone, which indicates the presence of fibrous tissue.

Figure 8 Back scatter image and X-ray microanalytical mapping of a titanium coated PMMA implants. (A) The implant with the titanium coating (white line) can be recognized. Bone surrounds the implant. Mapping for titanium (B), calcium (C), phosphorus (D), and carbon (E). (F) An integral image in which all different mappings are combined shows the presence of a bone-free zone at the implant interface.



Discussion

The aim of the present study was to determine whether the use of titanium coated polymeric implants allows an accurate examination of the bone implant interface μCT analysis The obtained data were compared with light microscopical and scanning electron microscopical (elemental mapping) data

Comparison of all results confirms that indeed the use of thin titanium coatings provides an alternative approach to prevent the occurrence of streaking artifacts and blurring of the implant surface as associated with bulk titanium implants On the other hand, it has to be noticed that the resolution of μCT-images is still significantly less compared with both used microscopical techniques, which excludes evaluation at the cellular level In view of this, additional visualization approaches are still needed for a proper complete study of the bone-implant response

Previous studies already confirmed that the composition of thin magnetron sputtered Ti-coatings is very similar to the surface composition of bulk titanium implants (Walboomers *et al* 2004) Rutherford backscattering spectroscopy and X-ray photoelectron spectroscopy indicated that sputtered Ti-coatings consist of titanium and oxygen in amounts of 1 1 Also, the adhesion property of this type of coating is sufficient to withstand continuous stretching at a frequency of 1Hz and a magnitude of 1000 μstrain

The overall bone response to titanium coatings is further very similar to other studies with Ti-coated polymeric implants For example, Albrektsson *et al* (1982) used cylindrical, non-threaded polycarbonate plastic implants coated with titanium or gold, which were inserted for 12 weeks into the tibia of rabbits The thickness of coating was 200-300 nm Using transmission electron microscopy, the bone surrounding the titanium-covered plastic core was shown to possess "normal" ultrastructural characteristics At the titanium interface, the last 2 or 3 lamellae of bone became arranged parallel to the surface of the central plastic plug and not concentrically as in Haversian systems The mineralization was reduced close to the interface (0 1-0 5 μm from the metal border) and the collagen bundles became replaced by filaments, randomly arranged close to the interface The last 20-40 nm from the titanium surface lacked distinct collagen filaments This zone was observed to consist of partly calcified amorphous ground substance and partly proteoglycans and glucoseaminoglycans No fibrous tissue was interposed between the bone and titanium surface These results were confirmed in several follow-up studies of the same group, where titanium coated implants were compared with zirconium (Albrektsson *et al* 1985) and stainless steel coatings (Albrektsson & Hansson 1986) Considering the intervening fibrous tissue layer in areas where the coating is lacking, our findings corroborates with a previous study of Ooms *et al* (2003) They injected PMMA bone cement into cortical bone defects as made into the tibia of goats After 2 weeks of implantation, fibrous tissue formation was observed at the bone-PMMA interface, which was still present after 12 weeks of implantation It has to be emphasized that the fibrous tissue response around this injected PMMA material was more enhanced compared to our exposed PMMA surface Probably, this is due to the manufacturing process of our implants The current implants were machined with a lathe out of pre-polymerized PMMA rods, while in the Ooms study the PMMA implants had to polymerize in situ, which results in prolonged release of cytotoxic monomer This explanation is supported by other studies (Schaffer 1999, Liu 2000, Fini 2002, Aho 2004), who all used pre-polymerized implants, which evoked a moderate non-compatible bone response characterized by the occurrence of reduced bone contact and a thin separating fibrous tissue layer

In our experiment, a conventional press-fit surgical technique was used for the installation of the implants Occasionally, we experienced that increased force was required to get the implants in the proper position This might be the reason for the locally observed absence of the Ti-coating Apparently, the tibial cortex of a goat is not the most optimal location for Ti-coated PMMA implants and low density trabecular bone, like as present in the femoral condyle or maxilla, has to be preferred

Various microscopical techniques can be used to study the tissue reaction to implants, including light microscopy, scanning electron microscopy, transmission electron microcopy and confocal laser scanning microscopy All these techniques provide information at the cellular level, but do not provide information about the elemental composition X-ray mapping is a technique that exists already for more than 40 years whereby an image is formed using an X-ray signal in order to illustrate the elemental distribution within a tissue sample (Sigee *et al* 1993) Under certain conditions, X-ray microanalysis is of special value in studies dealing with bone apposition on implants Unfortunately, during the last 10 years the interest and importance of this technique for biomaterials research has somewhat faded away However, the results as obtained in the current study prove again that scanning electron microscopy in combination with X-ray microanalysis is very valuable to prove the interfacial composition, i.e. the presence of bone.

In conclusion, the obtained results proof the final use of titanium coated PMMA implants for evaluation of the bone-implant response using µCT. However, this study also confirms that for a proper analysis of the bone-implant interface the additional use of microscopical techniques is still required.

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Chapter 8

Summary, general conclusions and future perspectives

Summary, general conclusions and future perspectives

The currently available experimental data do not provide a clear answer on the final value of surgical technique for oral implant fixation. Therefore, it was the aim of the studies presented in this thesis to investigate the effect of the used implant installation technique in relation to implant surface roughness on the final bone fixation. For this purpose, the following questions were addressed:

1. Does a higher implant surface roughness lead to a higher bone-to-implant contact?
2. Is a higher implant surface roughness result in a higher implant torque resistance?
3. Is surgical technique one of the major parameters for the final implant-bone behavior and perhaps more important than implant surface parameters, like roughness and composition?
4. Can a particular surgical technique increase the survival rate of implants?
5. What are the affects of the used surgical technique on the final implant fixation and bone behavior?

Summary

To get insight in the present evidence regarding implant surface roughness, a systematic review was performed on studies investigating implant surface roughness effects on bone response and implant fixation **(Chapter 2)**. Over 5900 abstracts on dental implant research were found in the MEDLINE. Subsequently, after application of inclusion/exclusion criteria, 470, 23, and 14 were articles included in the first, second and third selection steps, respectively. Almost all papers showed an enhanced bone-to-implant contact with increasing surface roughness. Also, a significant relation was found between push-out strength and surface roughness. Unfortunately, the eventually selected studies were too heterogeneous for inference of data. However, based on the primary studies it was concluded that the available data provided supportive evidence for a positive relationship between bone-to-implant contact and surface roughness.

Subsequently, in **Chapter 3**, using an in vitro model, the effects of implant surface roughness and surgical technique on implant fixation were investigated For this purpose, conical-shaped implants with machined or etched surface topography were implanted into the explanted femoral condyle of goats The implant sites were prepared either by a conventional technique, by undersized preparation, or by the osteotome technique Peak insertion & removal torque, bone-to-implant contacts and morphological bone appearance were assessed by scanning electron microscope and micro-computer tomography We found that insertion and removal torque values were significantly higher for etched implants inserted with the undersized technique (115 2 +/- 31 1, 102 9 +/- 36 4 N cm) respectively Further, the average bone-to-implant contact value was higher for the etched implants placed with the undersized technique (87 5 +/- 5 6), which was statistically significant compared with machined and etched implants inserted by conventional technique From this experiment, we conclude that the surgical technique has a decisive effect on implant fixation in trabecular bone

The systematic review presented in **chapter 4** was done to estimate the survival rate of implants inserted with osteotome technique The literature was searched using MEDLINE from 1953 to 2005 The literature search revealed 164 hits The inclusion criteria were clinical studies or clinical reports investigating the osteotome technique for dental implantation and control or test group(s) from clinical studies or clinical reports After the first selection step, 13 articles remained while151 were excluded Inclusion criteria in the second step were clinical studies or clinical reports using "osteotome technique" with dental implants and osteotome technique as used for implant site preparation with or without sinus floor elevation The second step revealed five papers fulfilling the inclusion criteria By pooling the data of the included studies, overall Kaplan-Meier survival curves were constructed for the periods before loading and after loading The combined data of 349 implants revealed survival probabilities of 98% (CI 97 2% - 100%) until loading and 99% (CI 94% - 100%) after 56 months of loading, respectively

We concluded that, the prognosis of implants inserted by osteotome technique as computed in this study seems to be similar to published data of implants that are inserted by conventional drilling technique

As a result of the *in vitro* study on the influence of the surgical technique on implant fixation in trabecular bone, an *in vivo* experiment was described in **chapter 5**. In this mechanical study, 48 conical implants with machined or etched surface topography were placed into the femoral condyle of goats. The implant sites were prepared either by a conventional, under-sized and osteotome technique. Evaluation of the interface strength and appearance, using torque test and scanning electron microscopy, was done a period of 12 weeks after implantation. Removal torque value of the etched implants placed with the undersized technique (98 ± 29Ncm) was statistically significantly higher compared to machined surface implants inserted by osteotome technique. SEM showed that all implants showed interfacial bone contact. In addition, the torque test in all experimental conditions resulted in fracturing at the bone-implant interface. Therefore, we conclude that the installation of etched implants using an undersized preparation of the implant bed results in superior bonding strength with the surrounding bone.

Thereafter, in **chapter 6,** the histological results of the influence of implant surface topography and surgical technique on bone response were described. For this experiment, 48 conical designed implants were used with two different surface finishes, i.e.: machined and etched. The implants were inserted in the left and right medial femoral condyle of 8 goats using three different surgical approaches: press-fit (implant diameter = implant bed diameter), undersized (implant bed diameter < implant diameter) and osteotome. Each femoral condyle received 3 implants. After healing period of 12 weeks the implants were retrieved and prepared for histological and histomorphometrical evaluation (bone contact and bone mass)

Light microscopy revealed that in general the bone response to all implants was very similar. On the other hand, histomorphometry suggested that the bone-to-implant contact for the etched implants inserted by an undersized technique was higher compared with machined implants and the other surgical approaches. The observed differences however, were not significant. Bone mass measurements did not reveal the occurrence of clear differences between groups with different surgical approaches. Supported by our findings, we conclude that an undersized preparation technique in trabecular bone with an etched implant surface supported an enhanced bone-implant contact in this model.

In **chapter 7,** polymeric implants were used to evaluate the bone response by microcomputer tomography (µCT) The implants had a machined threaded appearance and were provided with a 400-500 nm thick titanium coating The implants were inserted in the tibia of goats After healing period of 12 weeks the implants were retrieved and prepared for µCT, light microscopy, and X-ray microanalysis
The 3-D reconstructed representations showed clearly the implants surrounded by cortical bone No streaking artifacts were present The bone was found to have grown into the screw-threads and bone conduction into the marrow cavity was seen The histological evaluation demonstrated that the titanium-coated implants were well tolerated by the tissues In addition, the bone was seen in direct contact with the titanium-coated layer The X-ray microanalysis shows the presence of calcium and phosphorus which indicates the presence of bone The X-ray microanalysis results confirmed the light microscopic data At the end, the obtained results prove the use of titanium-coated PMMA implants for evaluation of the bone-implant response using µCT However, this study also confirms that for a proper analysis of the bone-implant interface the additional use of conventional microscopic techniques is still required

General conclusions

Although, oral implants are overall successful and already widely applied in clinical dental practice, still more basic knowledge is needed on the optimal implant material, design and surface characteristics in relation to the applied surgical technique as used for implant installation This becomes especially relevant, because there is a tendency to apply oral implants in more challenging situations, which are more prone to failure
Many variations in the surgical technique for the placement of dental implants in combination with different implants system have been developed since the introduction of implant surgery into clinical practice Yet, their interrelation is not understood in detail
The results of the investigations described in this thesis are discussed in this chapter Finally, based on these general conclusions, some recommendations for future research are made

In this thesis two distinct research methods were followed aiming to gain further insight in the effect of implant installation technique on the final oral implant fixation: one is the analysis of the available knowledge by means of two systematic reviews, the other is a series of in vitro and in vivo experimental studies.
The systematic review of animal studies we performed to investigate the effect of implant surface roughness on bone response and implant fixation revealed substantial heterogeneity in methods and results used in the studies included (Chapter 2). This heterogeneity has been caused by a number of variables:

1. Differences in study design. Differences between healing times in animal's models, variance of local bone quality and density, use of different implant systems, and variability of biomechanical tests prevent direct correlation of these parameters to the outcome of the clinical results.
2. Variation in the *in vivo* animal model as well as implant location within the same animal model. Local bone conditions and implant location vary between various animal species, which can have effect on the results of implant bone response studies.
3. Different methods and devices as used for roughness measurements. The different methods used in the various studies hamper a correct comparison of the obtained data.
4. Different surgical approaches for implant installation This is especially relevant when the last drill as used before implantation is smaller than the implant diameter.
5. Inadequate surgical technique description. Modifications in surgical technique strongly affect the bone behavior around the implant.
6. Different biomechanical tests in combination with different implant designs. The shape of the implant system is always an additional issue in the selection of a biomechanical test. Additionally, the interpretation of biomechanical tests has been shown to be difficult for implant materials with different Young's moduli.

Unfortunately, due to this heterogeneity it was not possible to synthesize the data by means of a meta-analysis (quantitative systematic review), nevertheless we were able to describe some relationships. To minimize heterogeneity, a series of even more detailed inclusion and exclusion criteria could have been set. However, too few studies would have remained to analyze properly The only way to deal with this problem is to further standardize experimental studies It is considered that this review provided some useful suggestions for minimal criteria in reporting investigations on this topic

A second systematic review was focusing on a specific implant insertion technique the osteotome technique (Chapter 4) It appeared to be impossible to get a clear answer regarding the value of the osteotome technique on the basis of the experimental data in the literature Fortunately, several clinical studies have been published describing the use of the osteotome technique for the installation of oral implants in the human maxilla Although the number of papers reviewed was limited and, again, the variation in study designs was substantial, it was possible to construct an overall survival rate of implants fixed with this technique None of the reviewed articles was designed as a randomized controlled clinical trial, so direct comparison with conventional drilling insertion techniques was not allowed Nevertheless, it was found that the prognosis of implants inserted by osteotome technique was in the same range as the prognosis published for implants that were inserted by conventional drilling techniques Although this systematic review could not reveal particular success or risk factors, we considered the osteotome technique a viable treatment option in selected cases

In our *in vitro* and *in vivo* experimental studies, goats were used The implants were installed in femoral condyles Although the femoral trabecular bone is supposed to resemble human maxillary bone, we observed a wide variation in bone quality in this model In addition, we have to notice that previous studies of our research group (Caulier 1996) already showed that, in contrast to the femoral condyle, the maxilla of a goat lacks a distinct cortical layer As a consequence, extrapolation of our data to the human situation is complex

In addition to the used bone model variable, we noticed that the osteotome surgical technique is difficult and requires guidance as well as extensive skill from the surgeon Improper orientation of the osteotome instrument can result in widening of the implant receptor site in the apical area causing decreased implant fixation Furthermore, when this technique is used together with an undersized preparation of the implant bed, there is still a lack of knowledge about the magnitude of stress as generated on the surrounding bone This is very relevant, because this can have a negative effect on the final bone response. Nevertheless, it was possible to draw some conclusions: (1) without knowing to which extent, surgical technique has shown to have a decisive effect on implant fixation in vitro (Chapter 3), (2) early mechanical fixation of etched implants seems to be improved when combined with undersized preparation. This seems to be not the case with machined implants surfaces (Chapter 5), and (3) the undersized preparation technique tends to improve bone-to-implant contact for both machined and etched implant surfaces in vivo. However, due to the power of the experiment statistical significance could not been demonstrated (Chapter 6).

Future perspectives

Currently there seems to be an overemphasis on implants hardware modification. Along with these modifications several changes in surgical equipment were introduced. During implantation the clinician is always aiming to find the best 'solution' for the specific 'problems' he is dealing with in that particular situation. A better documentation of all variables and their interrelations with clinical situations is necessary to increase the understanding in the possible effects following the implementation of these new techniques. For that, it is recommended to systematically, carefully and periodically review all literature data from clinical studies investigating the effect of different surgical implantation procedures in combination with different implant system. It would be worthwhile to create a databank providing this information and making it available for all clinicians.

Besides the more general recommendation above, emphasis should be directed to a better understanding of a few particular variables. One of these variables is the optimal ratio between drill receptor site, implant diameter and the subsequent biomechanical adaptation to stress. It is expected that further investigation of the required amount of bone-stress induced by this variable will optimize implant-bone fixation.

Standardization of surface roughness measurement methods for implants will strongly enhance understanding of underlying mechanisms in relation with surgical parameters. Without a standard procedure, it is generally impossible to compare outcomes between studies (Wennerberg and Albrektsson 2000).

Using bone tissue from animals for *in vitro* mechanical studies is scientifically speaking an excellent choice However, extrapolation of the results is hampered by a discrepancy in bone density between animals and humans Therefore, the use of artificial bone offers the possibility to vary the bone quality parameters in a more reliable and standardized (*i e* , sawbones) and can be used as system model for *in vitro* implant studies (Flahiff *et al* 1995, Fujishiro *et al* 2005, Beckmann *et al* 2006, Madsen and Haug 2006, Pekmezci *et al* 2006)

With different implant designs (*i e* , cylindrical, screw shape), different biomechanical tests should be applied Micro-computer tomography could be use as a predictor and structural analysis of trabecular bone around the implant before and after implantation procedures (Majumdar *et al* 1998, Wachter *et al* 2001, Bauer *et al* 2006, Guerrero *et al* 2006) This could possibly eliminate the use of biomechanical tests, which is in fact a more or less incomplete and derived measurement method to assess biological adaptation

Titanium is considered as a bioinert material, while calcium phosphate ceramics are bioactive For example, it is known that calcium phosphate-coated implants favor the bone response and can have an additional effect in enhancing implant bone fixation (Maxian *et al* 1994, Hulshoff and Jansen 1997, Wolke *et al* 2003, Cimerman *et al* 2005) Consequently, this additional parameter has to be included in future studies to oral implant fixation

Considering the above mentioned, the successful combination of both the clinician's experience as well as the biomaterial's science knowledge, subsequent incorporation into new therapeutically approaches is one of the big challenges for the future Only then it will be possible to further develop a more efficient oral implant treatment protocol

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Summary in Dutch

Samenvatting, algemene conclusies en toekomst verwachtingen

Tot nu toe geeft de wetenschappelijke litteratuur ons nog niet voldoende antwoord gegeven over het belang van de chirurgische techniek voor het uiteindelijke succes van tand implantaten Het doel van de studies die beschreven worden in dit proefschrift is om het effect te bepalen van de techniek die gebruikt wordt om tand implantaten te plaatsen in relatie tot de ruwheid van het implantaatoppervlak en de uiteindelijke fixatie van het implantaat in het kaakbot Daartoe werd een antwoord gezocht op de volgende vragen

Leidt een ruwer implantaatoppervlak tot een beter contact tussen bot en implantaat ?

Leidt een ruwer implantaatoppervlak tot een hogere torque weerstand?

Is de chirurgische techniek éen van de belangrijkste factoren voor osseointegratie en misschien zelfs belangrijker dan oppervlakte ruwheid en samenstelling van het implantaat?

Kan een bepaalde chirurgische techniek de overlevingsduur van implantaten verbeteren?

Beinvloedt de chirurgische techniek de botfixatie van het implantaaat en het bot gedrag?

Samenvatting

Om inzicht te krijgen in de kennis die reeds beschikbaar is over het effect van implantaatoppervlakte ruwheid, werd eerst een systematische review uitgevoerd van studies waarin het effect van implantaatoppervlakte ruwheid op het botgedrag beschreven werd Voor **(Hoofdstuk 2)** werden meer dan 5900 abstracts gelezen die te maken hadden met onderzoek naar tand implantaten Nadat inclusie en exclusiecriteria waren toegepast bleven er nog 470 artikelen over, dat na een 2^e en 3^e selectiestap teruggebracht werd tot respectievelijk 23 en 14 artikelen De grote variatie in de data maakte uiteindelijk een meta-analyse onmogelijk De meeste artikelen lieten echter een significante relatie tussen bot-implantaat contact en oppervlakteruwheid zien Helaas waren de geselecteerde artikelen te heterogeen voor het vergelijken van de data Gebaseerd op de primaire studies werd echter geconcludeerd dat er op basis van de beschikbare gegevens voldoende bewijs is dat een positieve relatie aanwezig is tussen bot-implantaat contact en oppervlakteruwheid

Vervolgens werd in **(Hoofdstuk 3)** een in-vitromodel gebruikt om het effect van oppervlakteruwheid en chirurgische techniek op implantaat fixatie te onderzoeken Hiervoor werden schroefvormige tand implantaten met een glad of geetst oppervlak geimplanteerd in het trabeculaire bot van een geexplanteerde femurkop van geiten Voor het plaatsen van de implantaten werden drie verschillende chirurgische technieken gebruikt (1) een conventionele techniek, (2) ondermaats boren van het gat in het bot in relatie tot de implantaat diameter en (3) een osteotoom techniek De inschroef- en uitdraaiweerstand, bot-implantaat contact en botmorfologie werden beoordeeld met behulp van mecahnische apparatuur, scanning electronen microscopie (SEM) en micro-computertomografie (micro CT) De inschroef- en uitdraaiweerstand bleken significant hoger te zijn voor implantaten die vorozien waren van een geetst oppervlak en geplaatst werden met de "ondermaatse" preparatietechniek (respectievelijk 115 2 +/- 31 1, 102 9 +/- 36 4 N cm) Verder was ook de gemiddelde waarde van het bot-implantaatcontact sigficant hoger voor de geetste implantaten geplaatst met de "ondermaatse" techniek (87 5 +/- 5 6 N cm) vergeleken met gladde en geetste implantaten geplaatst met de conventionele techniek Er werd daarom geconcludeerd dat de chirurgische techniek een duidleijk effect heeft op fixatie van een tand implantaat in trabeculair bot

De systematische review in **(Hoofdstuk 4)** werd gedaan om meer informatie te verkrijgen over de klinische overlevingsduur van tand implantaten, die geplaatst worden met behulp van een osteotoom techniek De literatuur tussen 1953 en 2005 werd doorzocht door middel van Medline Er werden 164 artikels gevonden De inclusiecriteria waren klinische studies of verslagen die de osteotoom techniek onderzochten voor tand implantaten evenals test of controle groepen, zelfs als deze niet volledig aan de andere voorwaarden voldeden Na de 1^e selectiestap bleven 13 artikels over en werden er 151 uitgesloten Het 2^e inclusiecriterium was klinische studies of verslagen die de osteotoom techniek onderzochten voor tand implantaten en waarin de osteotoomtechniek gebruikt werd voor het voorbereiden van de implantaat plaatsing met of zonder sinuslift Na de 2^e selectiestap bleven er nog 5 artikelen over die voldeden aan de inclusiecriteria Door deze data samen te voegen konden Kaplan-Meier overlevings curves worden berekend voor de periodes voor en na het belasten van de implantaten De gecombineerde gegevens van 349 implantaten toonden overlevingskansen van respectievelijk 98% (CI 97 2% - 100%)

tot aan de belasting en 99% (CI 94% - 100%) na 56 maanden belasting Aan het einde van de observatieperiode waren er nog 41 implantaten (18 patienten) waarvan het niet geheel duidelijk was of zij succesvol waren
We concludeerden dat de prognose van implantaten die geplaatst worden met behulp van een osteotoomtechniek gelijk is aan die van tand implantaten welke geplaatst worden met behulp van een conventionele techniek

Gezien de belangrijke invloed van de chirurgische techniek op de fixatie van een tandimplantaat in trabeculair bot werd een in vivo studie uitgevoerd welke beschreven is in **(Hoofdstuk 5)** In deze mechanische studie werden 48 geschroefde implantaten met een glad of geetst oppervlak geplaatst in de femorale condyle van geiten De implantaten werden geplaatst middels een zg conventionele, “ondermaatse” en osteotoom preparatietechniek De mechanische sterkte en morfologie van het bot-implantaat scheidingsvlak werden 12 weken na implantatie geevalueerd met een torque test en SEM De uitschroeftorque van de “ondermaats” geplaatste geetste implantaten bleek significant hoger (98 ± 29Ncm) te zijn vergeleken met de gladde implantaten geplaatst met de osteotoom techniek SEM liet zien dat rondom alle implantaten het bot in direkt contact was met het implantaatoppervlak Daarbij resulteerde de torque test in alle experimenten in breuk van het scheidingsvlak implantaat-bot Op basis van de resultaten werd geconcludeerd dat het plaatsen van geetste implantaten met een “ondermaatse” preparatietechniek resulteert in een sterkere hechting met het omgevende bot

Vervolgens werden in **(hoofdstuk 6)** de histologische resultaten van de invloed van implantaat oppervlakte topografie en chirurgische techniek op botreactie beschreven Voor dit experiment werden 48 schroefvormige implantaten met een glad of ruw oppervlak gebruikt De implantaten werden geplaatst in de rechter en linker mediale femorale condyle van 8 geiten Hierbij werden drie verschillende chirurgische technieken gebruikt namelijk press-fit (diameter implantaat =diameter preparatie), “ondermaats (diameter implantaat is groter dan diameter preparatie) en osteotoom techniek In elke condyle werden 3 implantaten geplaatst Na een implantatieperiode van 12 weken werden de implantaten met het omringende bot verwijderd en verwerkt voor histologische en histomorfometrische evaluatie (botcontact en botmassa)

Licht microscopisch onderzoek toonde aan dat de botreactie rondom alle implantaten gelijk was De histomorfometrische metingen leken aan te tonen dat het botcontact met de geetste "ondermaats" geplaatste implantaten groter was dan voor de gladde implantaten en andere chirurgische technieken, maar de gemeten verschillen bleken niet significant te zijn Ook de botmassa metingen toonden geen duidelijke verschillen tussen de groepen Gebaseerd op deze bevindingen werd geconcludeerd dat in dit model een "ondermaatse" preparatie in trabeculair bot voor geetste implantaatoppervlakken in een beter bot-implantaatcontact resulteert

In **hoofdstuk 7,** werden plastic implantaten gebruikt om de botreactie te evalueren met micro CT De implantaten hadden een glad geschroefd oppervlak en waren bedekt met een 400-500 nm dikke titanium coating De implantaten werden geplaatst in de tibia van geiten Twaalf weken na implantatie werden deze implantaten met omringend bot verwijderd en en verwerkt voor micro CT, lichtmicroscopie en Ronten micro-analyse De gereconstrueerde 3D-toonden duidelijk aan dat de implantaten omgeven waren door corticaal bot Er waren geen noemenswaardige artefacten zichtbaar Het bot was in de schroefdraad ingegroeid en botgeleiding over het implantaat oppervlak was zichtbaar tot in het beenmerg De histologische evaluatie liet zien dat de titanium gecoate implantaten goed door de weefsels werden getolereerd Dit was zichtbaar door de aanwezigheid van een direct contact tussen botweefsel en titanium coating De rontgen micro-analyse toonde de aanwezigheid van calcium en fosfor wat het bot-achtige karakter van het omringende weefsel bevestigt De rontgenmicro-analyse resultaten kwamen goed overeen met de lichtmicroscopische beelden De resultaten bewijzen dat titanium gecoate plastic implantaten gebruikt kunnen worden voor de evaluatie van het bot-implantaat contact met behulp van micro CT Deze studie bevestigde echter ook dat voor een volledige analyse van het bot-implantaat scheidingsvlak niet alleen vertrouwd kan worden op micro CT, maar dat het gebruik van aanvullende conventionele microscopische technieken nodig is

In **hoofdstuk 8** worden de slotconclusies gemaakt en worden aanbevelingen voor toekomstig onderzoek gegeven

Algemene conclusies

Hoewel tandheelkundige implantaten in het algemeen erg succesvol zijn, is toch nog meer onderzoek nodig naar de optimale implantaatvorm en het effect dat de oppervlakte eigenschappen hebben op het botgedrag in relatie tot de gebruikte chirurgische techniek Dit is met name belangrijk omdat er een tendens is om implantaten steeds meer te gaan toepassen in complexe situaties waar de kans groot is dat het implantaat mislukt

Verschillende chirurgische technieken, samen met verschillende implantaatsystemen, zijn ontwikkeld sinds de introductie van tandimplantaten Hoe deze twee parameters zich echter tot elkaar verhouden is niet duidelijk De resultaten van de diverse onderzoeken die in dit proefschrift beschreven zijn, worden in dit hoofdstuk verder besproken

Tenslotte worden er, gebaseerd op de algemene conclusies, aanbevelingen gegeven voor verder onderzoek

In dit proefschrift werden twee aparte onderzoeksstrategien gebruikt om meer inzicht te krijgen in het effect van de techniek die gebruikt wordt om een implantaat in het kaakbot te plaatsen en de uiteindelijke fixatie van dit implantaat Eén daarvan is de analyse van de beschikbare kennis door systematische reviews, de andere is een serie van in vitro en in vivo experimentele studies

De systematische review van proefdieronderzoek werd gedaan om het effect van oppervlaktestructuur op zowel botrespons als implantaatfixatie te onderzoeken De resultaten van deze review lieten echter een grote heterogeniteit van de beschikbare gegevens zien (hoofdstuk 2), welke veroorzaakt werd door verschillende factoren

1 Verschil in studie onderwerp Verschillen in de inhelingsperiode in gebruikte diermodellen, verschil in locale botkwaliteit en densiteit, gebruik van verschillende implantaatsystemen en biomechanische testen, maakten een directe correlatie van deze parameters met de klinische resultaten onmogelijk

2 Verschil in de gebruikte diermodellen en ook de verschillende implantaatlocaties wanneer wel hetzelfde diermodel gebruikt werd Locale botcondities en implantaatlocatie verschillen tussen verschillende dieren, wat uiteindelijk een effect kan hebben op de implantaat-botreactie

3 Verschillende methodes en meetinstrumenten om de oppervlakteruwheid van een implantaat te meten Dit maakt een goede vergelijking van de gegenereerde data buitengewoon moeilijk

4 Het gebruik van verschillende chirurgische technieken voor het plaatsen van het implantaat Dit is vooral belangrijk wanneer de laatste boor zoals gebruikt wordt om het implantaat bed te prepareren kleiner is dan de diameter van het implantaat

5 Het niet neschibaar zijn van voldoende gegevens over de toegepaste chirurgische techniek Verschillen in chirurgische techniek kunnen een zeer groot effect hebben op het botgedrag rondom het implantaat

6 Verschillende biomechanische testen in combinatie met verschillende implantaatvormen De vorm van een implantaatsysteem is altijd een bijkomend probleem in de keuze van een bepaalde biomechanische test Tevens is de interpretatie van de uitkomst van een biomechanische test zeer moeilijk voor implantaten (materialen) met een verschillende Young's modulus

Helaas was het door deze heterogeniteit niet mogelijk om de data door middel van meta-analyse te bewerken (kwantitatieve systematische review) Het was echter wel mogelijk om sommige relaties te beschrijven Om heterogeniteit te verkleinen hadden ook nog meer inclusie-of exclusiecriteria toegepast kunnen worden Er zouden dan echter te weinig studies voor een goede analyse zijn overgebleven De uiteindelijke slotconclusie was dat deze review bruikbare suggesties opleverde voor minimale criteria waaraan rapportages over dit onderwerp moeten voldoen

Een tweede systematische review richtte zich op een specifieke implantatietechniek de zg osteotoom techniek (Hoofdstuk 4) Het bleek helaas onmogelijk om op basis van de beschikbare literatuur gegevens een duidelijk antwoord te krijgen over het nut van de osteotoom techniek Gelukkig zijn er echter wel diverse klinische studies gepubliceerd over het gebruik van de osteotoomtechniek voor het plaatsen van implantaten in de bovenkaak Hoewel het aantal studies beperkt was en er vesrchillen bestonden in het ontwerp van de diverse onderzoeken, kon toch een totale overlevingstijds berekend worden voor de implantaten die met deze techniek geplaatst werden Geen enkele van de onderzochte artikelen was echter gebaseerd op gerandomiseerd klinisch onderzoek, waardoor een directe vergelijking met de conventionele implantatietechniek niet mogelijk was Desalniettemin werd gevonden dat de prognose voor implantaten, die geplaatst worden met de conventionele techniek, vergelijkbaar is met die van de osteotoom techniek Hoewel deze systematische review geen duidelijke succes- of risicofactoren liet zien, kan toch gesteld worden dat de osteotoomtechniek een goede behandelwijze is voor de hiervoor geeigende situaties

Voor de in vitro en in vivo experimenten werden geiten gebruikt De implantaten werden geplaatst in de femorale condyle Hoewel het trabeculair bot van de geitenfemur lijkt op dat van de mens, bleek toch een grote variatie in botkwaliteit te bestaan Daarbij moet tevens opgemerkt worden dat eerder onderzoek (Caulier 1996) al heeft laten zien dat het bot in de bovenkaak weten van geiten geen duidelijke corticale laag heeft Dit maakt de extrapolatie van de resultaten naar de menselijke situatie zeer moeilijk

Naast een probleem met het botmodel, werd ook gevonden dat de osteotoom techniek moeilijk is en dat uitgebreide ervaring van de chirurg wenselijk is Een slechte orientatie van het osteotoom instrument kan leiden tot een verbreden van de receptorplaats in het apicale gedeelte wat weer leidt tot een verminderde implantaatfixatie Verder is het nog onduidelijk hoe groot de spanning is die op het bot wordt uitgeoefend dat het implantaat omgeeft, wanneer deze techniek gebruikt wordt in combinatie met een ondermaatse prepatietechniek Dit is echter zeer belangrijk omdat teveel spanning een negatief effect kan hebben op de botreactie

Toch konden een paar conclusies getrokken worden (1) de chirurgische techniek heeft een duidelijk effect op implantfixatie in vitro (hoofdstuk 3), (2) de vroege mechanische fixatie van geetste implantaten lijkt verbeterd te worden door gebruik te maken van een ondermaatse preparatietechniek (hoofdstuk 5), en (3) de ondermaatse preparatietechniek lijkt het bot-implantaatcontact te verbeteren voor zowel geetste als gladde implantaatoppervlakken in vivo Echter door een te kleine groepsgrootte kon geen statistische significantie worden aangetoond (hoofdstuk 6)

Toekomstperspectieven

De laatste tijd wordt er steeds meer aandacht besteed aan de veranderingen aan het implantaat zelf Van de andere kant zijn verschillende veranderingen in de chirurgische techniek geintroduceerd Tijdens de implantatie probeert de chirurg steeds de beste ‘oplossing’ te vinden voor de desbetreffende situatie Een betere beschrijving van alle variabelen en hun onderlinge relatie met klinische situaties is nodig om beter de mogelijke effecten te begrijpen die deze veranderingen veroorzaken Een aangewezen methode is het systematisch en zorgvuldig raadplegen van de literatuur Het zou dan ook goed zijn wanneer er een databank zou komen waarin alle informatie betreffende implantatietechniek en implantaat systeem beschikbaar zou komen

Naast deze algemene aanbevelingen, willen we toch ook een paar variabelen beter benadrukken Eén van deze variabelen is de optimale ratio tussen de boor die gebruikt wordt voor de preparatie van de implantaat receptor plaats en de diameter van het implantaat Verder onderzoek naar de hoeveelheid "spanning" die door deze discrepantie in diameter wordt opgewekt, kan het bot-implantaat gedrag verbeteren Standarizatie van de methode om oppervlakteruwheid te bepalen zal tot een beter begrip leiden van het effcet van deze parameter op het bot-implantaat gedrag Zonder een gestandarizeerde procedure blijft het onmogelijk om de resultaten van diverse sutdies met elkaar te vergelijken (Wennerberg and Albrektsson 2000)

Het gebruik van dierlijk botmateriaal voor in vitro mechanische studies is wetenschappelijk gezien een uitstekende keuze Gezien het verschil in botdichtheid tussen mens en dier is extrapolatie van de resultaten echter toch niet eenvoudig Het gebruik van kunstbot biedt echter de mogelijkheid om de botkwaliteit parameters wel te standardizeren Kunstbot kan dan ook prima gebruikt worden als model systeem voor in vitro implantaatstudies (Flahiff *et al* 1995, Fujishiro *et al* 2005, Beckmann *et al* 2006, Madsen and Haug 2006, Pekmezci *et al* 2006)

Voor verschillende implantaatvormen (cylindrisch vs schroefvorm) dienen ook verschillende biomechanische testen te worden gebruikt Micro-computer tomografie kan toepgepast worden om een structurele analyse van het trabeculair bot uit te voeren voor en na de implantatie (Majumdar *et al* 1998, Wachter *et al* 2001, Bauer *et al* 2006, Guerrero *et al* 2006) Wellicht dat dit zelfs het gebruik van biomechanische testen overbodig kan maken, omdat deze in principe een min of meer onvolledige meetmethode zijn om de biologische aanpassing van implantaten te onderzoeken

Titanium wordt beschouwd als een bio-inert material terwijl implantaten die gecoat zijn met calciumfosfaat de botrespons positief beinvloeden en een stimulerend effect hebben op de ingroei van het implantaat in het bot (Maxian *et al 1994*, Hulshoff and Jansen *1997*, Wolke *et al* 2003, Cimerman *et al* 2005) Daarom dient het effect van deze parameter meegenomen te worden in toekomstig onderzoek

De succesvolle combinatie van de ervaring van de chirurg en de kennis van de literatuur wat betreft biomaterialen en de hieruit voortkomende therapien is een grote uitdaging voor de toekomst Alleen dan is het mogelijk om een efficienter behandelprotocol te ontwikkelen

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Acknowledgement

This thesis is the result of three years of work whereby I have been accompanied and supported by many people Although it is not possible to mention everyone by name, I would like to express my gratitude to the following persons

The first person I would like to thank is my direct supervisor **professor dr. John Jansen.**

During these years I have known him as a sympathetic and principle-centered person His overly enthusiasm and integral view on research and his mission for providing 'only high-quality work and not less', has made a deep impression on me I owe him lots of gratitude for having me shown this way of research He could not even realize how much I have learned from him

My promotor **professor dr. Nico Creugers** who kept an eye on the progress of my work and always was available when I needed his advises I was more refreshed and excited at the end of every discussion with you I thank you for allowing me to benefit from your intellectual smartness

My co-promoter **dr. Joop Wolke,** I thank you for taking me so kindly and delicately Dear Joop, I am deeply obliged to you

My special thanks to **professor dr. Martin van't Hof** and **Mr. Jan Mulder** for the advice in methodology and for the great service in statistical analysis

I would like to thank all members of the Department of Biomaterials and Periodontology of the University Medical Centre Nijmegen for their friendship and hospitality to me in the past three years

I would like to express my thanks to the Ministry of Health in my country "Saudi Arabia" for the help and the scholarship that I got from them Their scholarship made it possible for me to do this project

My dear parents, thank you for your love and care in all these years Last but not least, I am greatly appreciative to my husband and my kids for their understanding, patience and support during the entire period of my study

Curriculum vitae

Manal Matouq Shalabi was born in Riyadh, Saudi Arabia on May 18^{th}, 1968

She went to the secondary school from 1976 to 1988 Then she studied dentistry at King Saud University (Saudi Arabia) from 1988 to 1992 She fulfilled her internship Program (Dental college, King Saud University), from 1992 to 1993 From 1993 to 2000 she practiced general dentistry at Riyadh Medical Complex (Ministry of Health)

In 2000 she enrolled in the Periodontology postgraduate training program at the University of Nijmegen (The Netherlands), from 2000 to 2003 Then, from September, 2000 she started her PhD project at the department of Biomaterial and Periodontology, University Medical Center Nijmegen (The Netherlands)

Summary in Arabic

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يكون صعباً بسبب وجود تباين في كثافة العظم بين الحيوان و الإنسان[7-3] . لذلك يقدم استخدام العظم الاصطناعي الإمكانية لحدوث تغير في المعالم النوعية للعظم أكثر موثوقية وقابلية للقياس مثل تحليل بنية العظم حول الغرسة قبل وبعد إجراءات الغرس. ويمكن لهذا الإجراء أن يلغي استخدام الاختبارات الميكانيكية الحيوية حيث تكون طريقة القياس المشتقة غير كاملة بشكل أقل أو أكثر لتحديد التكيف الحيوي للعظم[11-8] . يعتبر التيتانيوم مادة خاملة حيوياً بينما تكون مواد الحزف و الفوسفات و الكالسيوم نشطة حيوياً , فمثلاً من المعروف بأن الغرسات المطلية بطبقة من فوسفات الكالسيوم تكون أفضل لاستجابة العظم ويمكنها أن تمتلك تأثيراً إضافياً في تعزيز ثبات الغرسة في العظم [15-12]. وبناء على ذلك , يجب تصميم هذا المعلم الإضافي في الدراسات المستقبلية لثبات الغرسة.

إن أخذ ما سبق بعين الاعتبار والمشاركة الناجحة بين خبرة الطبيب السريري في المعرفة العملية للمادة البيولوجية وبالتالي التعاون في تطبيق الأساليب العلاجية الحديثة هي من التحديات الكبيرة للمستقبل , وعندما يكون هناك إمكانية لمزيد من التطوير , يجب وضع بروتوكول معالجة فعال في علم غرس الأسنان.

2) أظهر التثبيت الميكانيكي المبكر للغرسات المخرشة تحسناً عند مشاركتها مع طريقة التحضير المحدود الحجم للعظم حيث لم يلاحظ ذلك في حال استخدام الغرسات التي تم تحضير حشونة سطحها آليا (الفصل5).

3) تميل طريقة التحضير المحدود الحجم للعظم إلى تحسين اتصال الغرسة مع العظم للغرسات التي تم تحضير حشونة سطحها آلياً أو بالتحريش بالحمض لدى الأحياء .

وعلى كل , لا يمكن توضيح هذا التأثير بسبب قوة المعنوية الإحصائية لحجم الاختبار (أي لتقدير أرجحية أن تكون نتائج الدراسة حقيقية وليست وليدة المصادفة) (الفصل6).

نظرات مستقبلية

يبدو حالياً وجود مغالاة حول تعديل أدوات ومواد الغرسات. ومع هذه التعديلات تم التعرف إلى عدة تغييرات في التجهيزات المستخدمة في الجراحة , يهدف الطبيب السريري دائماً خلال عملية الغرس لإيجاد أفضل "حل" للمشاكل "النوعية" التي يتعامل معها في حالات خاصة . إن التوثيق الأفضل لكافة المتغيرات وعلاقاتهم مع الحلول السريرية هو ضروري لزيادة الفهم للآثار المحتمل حدوثها بعد عملية الغرس بتطبيق الطرق الجديدة. من أجل ذلك, يوصى بمراجعة بيانات الدراسات السريرية بشكل منتظم و دقيق و دوري لاستقصاء تأثير إجراءات الغرس الجراحية المختلفة و أشكال الغرسات المختلفة. ومن المفيد إنشاء بنك بيانات و معلومات تكون متاحة لجميع الأطباء السريريين.

إلى جانب التوصيات العامة العديدة السابقة , يجب توجيه التركيز نحو فهم أفضل لمتغيرات خاصة قليلة أحدها معرفة النسبة المثلى بين مكان إجراء الثقب في العظم وقطر الغرسة والتكيف الميكانيكي الحيوي اللاحق للإجهاد. ويتوقع بأن تقصيات إضافية للكمية المطلوبة من الإجهاد المحدث على العظم بواسطة هذا المتغير سوف يزيد من ثبات الغرسة مع العظم.

إن معايرة طرق قياس حشونة سطوح الغرسات سوف يعزز بقوة فهم الآليات الأساسية للعلاقة مع المعالم الجراحية. وبدون إجراء قياسي, من المستحيل بصورة عامة مقارنة النتائج بين الدراسات[2].

يظهر من الناحية العلمية , بأن استخدام النسج العظمية من الحيوانات في الدراسات الميكانيكية المخبرية هو خيار ممتاز إلا أن استقراء النتائج

الدراسات السريرية تصف استخدام طريقة قطع العظم لوضع الغرسات الفموية في فك الإنسان.

بالرغم من العدد المحدود للدراسات التي تمت مراجعتها , فقد كان هناك اختلاف جوهري في تصاميم الدراسات وكان من الممكن تحقيق نسبة عامة لديمومة الغرسات المثبتة بهذه الطريقة. لم تكن أي من المقالات التي تم مراجعتها مصممة كتجارب سريرية مُراقبة وعشوائية, لذلك كانت المقارنة المباشرة مع الطرق التقليدية في غرز الغرسة باستخدام المثقب غير ممكنة. وعلى كلٍ , لقد وُجد بأن إنذار الغرسات المغروزة بطريقة قطع العظم يسير .في نفس اتجاه إنذار الغرسات التي كانت قد غرزت بطرق الثقب التقليدية. بالرغم من أن هذه المراجعة المنتظمة لم تستطع أن تكشف نجاحاً خاصاً أو عوامل خطر, فإننا اعتبرنا بأن طريقة قطع العظم هي خيار علاجي قابل للتطبيق في بعض الحالات.

كان حيوان الماعز قد استُخدم في دراساتنا في المخبر وفي الأحياء و كانت الغرسات قد وضعت في لقمة عظم الفخذ . بالرغم أنه من المفترض أن يكون عظم الفخذ للماعز يشبه عظم الفك في الإنسان , إلا أننا لاحظنا وجود اختلاف كبير في نوعية العظم في الماعز عما هو في الإنسان. بالإضافة إلى ذلك, لاحظنا بأن الدراسات السابقة[1] في بحثنا هذا أظهرت تبايناً في نوعية لقمة عظم الفخذ وعظم الفك للماعز الذي يفتقد الطبقة القشرية الواضحة , و نتيجة لذلك كان تطبيق بيانات هذه الدراسة على الإنسان معقداً.

إضافة إلى نموذج العظم المتغير المستخدم , لاحظنا بأن طريقة قطع العظم الجراحية هي صعبة و تتطلب

مرشداً , إلى جانب مهارة كبيرة من الجراح. يمكن أن يؤدي التوجيه الخاطئ لأداة قطع العظم إلى اتساع في مكان وضع الغرسة في المنطقة الذروية مسبباً تناقصاً في ثبات الغرسة. وكذلك عندما تستخدم هذه الطريقة مع طريقة التحضير الأصغر حجما لمكان الغرسة , يبقى هناك نقص في المعرفة حول حجم الإجهاد المطبق على العظم المحيط بالغرسة, حيث يمكن أن يكون له تأثيراً سلبياً على استجابة العظم النهائية. وعلى كلٍ , أمكن وضع بعض الاستنتاجات وهي:

1) أظهرت الطريقة الجراحية المطبقة تأثيراً حاسماً على ثبات الغرسة في التجربة المخبرية ولكن بدون معرفة حجم هذا التأثير (الفصل3).

واستخدام أشكال غرسات مختلفة وتغير الاختبارات الميكانيكية الحيوية، مما يمنع من حدوث ربط مباشر لهذه المعالم مع حصيلة النتائج السريرية.

2- اختلاف في نماذج الحيوان في دراسة الأحياء وكذلك في مكان الغرسة في نفس نموذج الحيوان: تختلف شروط العظم الموضعية ومكان الغرسة بين أنواع الحيوانات المختلفة التي يمكن أن يكون لها تأثير على نتائج الدراسات المتعلقة باستجابة العظم حول الغرسة.

3- استخدام طرق وأدوات مختلفة لقياس الخشونة : إن تعدد الطرق المستخدمة في الدراسات المختلفة يعيق من إجراء مقارنة صحيحة للبيانات الناتجة.

4- تطبيق أساليب جراحية مختلفة لوضع الغرسة : ويظهر ذلك بشكل خاص عندما يكون قطر المثقب الأخير المستخدم قبل الغرس أصغر من قطر الغرسة .

5- الوصف غير الملائم للطريقة الجراحية : تؤثر التعديلات في الطريقة الجراحية بشكل قوي على سلوك العظم حول الغرسة مستقبلاً.

6- اختلاف الاختبارات الميكانيكية الحيوية ونماذج الغرسات: يكون شكل الغرسة دائما قصبة إضافية في اختبار الاختبار الميكانيكي الحيوي. إضافة إلى ذلك، كان تفسير الاختبارات الميكانيكية الحيوية صعبا بالنسبة لمواد الغرسة مع اختلاف مُعامل يونغ.

ولسوء الحظ، لم يكن ممكنا بسبب هذه التغايرية استخدام البيانات لإجراء تحليل تجميعي.(مراجعة منتظمة كمية)، ومع ذلك فقد استطعنا وصف بعض العلاقات بين المتغيرات المذكورة. وللإقلال من التغايرية حتى الحد الأدنى ، ثم وضع سلسلة من المعايير كانت أكثر تفصيلاً حول تصميم و استبعاد الدراسات من المراجعة. وعلى كل، تبقى هناك دراسات قليلة جداً يمكن تحليلها بشكل دقيق . إن الطريقة الوحيدة لمعالجة هذه المشكلة هي إجراء مزيد من الدراسات التجريبية القياسية. ويعتبر بأن هذه المراجعة أوجدت بعض المقترحات المفيدة للإقلال من المعايير في وضع التقارير الاستقصائية حول هذا الموضوع .

أما المراجعة المنتظمة الثانية فقد ركزت على استخدام طريقة نوعية في عزز الغرسة وهي: طريقة قطع العظم (الفصل4). لقد ظهر أنه من المستحيل الحصول على جواب واضح فيما يتعلق بقيمة طريقة قطع العظم على أساس البيانات التجريبية في المطبوعات المنشورة. ولحسن الحظ فقد نشر عدد من

وفي الخاتمة, فإن النتائج التي تم إحرازها تؤكد الاستخدام النهائي للغرسات المصنعة من ميثيل الراتين الأكريلي الجدول. المغطاة بالتيتانيوم لتقييم استجابة العرسة - العظم باستخدام الرسم الطبقي بالحاسوب . وعلى كل , تؤكد هذه الدراسة أيضا بأن التحليل الجيد لطبقة اتصال العرسة مع العظم مازالت تتطلب استخداماً إضافياً لطرق الفحص المجهري .

استنتاجات عامة

بالرغم, بشكل عام, من نجاح العرسات الفموية وتطبيقها الآن سريريا بشكل واسع في العيادات السنية, ما تزال هناك حاجة إلى معارف أساسية أكثر حول مادة الغرسة وتصميمها ومواصفات سطحها من حيث علاقتها بالطريقة الجراحية المطبقة لوضع العرسة في العظم. وقد أصبحت لهذه المعارف أهمية خاصة بسبب وجود اتجاه نحو تطبيق العرسات الفموية في الحالات الأكثر ارتيابا أي التي تكون أكثر عرضة للفشل في المستقبل .

تم تطوير الطرق الجراحية المستخدمة في وضع العرسات السنية وأشكال العرسات المختلفة منذ إدخال عرس الأسنان في الممارسة السريرية. وحتى الآن ما تزال العلاقات المتبادلة بينهما غير مفهومة بشكل تفصيلي.

تناقش في هذا الفصل نتائج الاستقصاءات الموصوفة في هذه الأطروحة وتُوضع بعض التوصيات المبنية على الاستنتاجات العامة من أجل البحوث المستقبلية.

هناك طريقتا بحث واضحتين في هذه الأطروحة تم إتباعهما بهدف الحصول على معارف أعمق لدراسة تأثير طريقة وضع العرسة الفموية على الثبات النهائي لها. الطريقة الأولى هي تحليل المعلومات المتوافرة من المراجعتين المنتظمتين, والثانية مراجعة نتائج سلسلة الدراسات التجريبية التي جرت في المخبر أو لدى الأحياء.

أوضحت المراجعة المنتظمة الأولى للدراسات التي جرت على الحيوانات لاستقصاء تأثير خشونة سطح العرسة على استجابة العظم وثبات العرسة وجود تغايرية جوهرية في الطرق و النتائج المستخدمة في الدراسات المذكورة مسببة عن عدد من المتغيرات وهي (الفصل2):

1- اختلافات في تصميم الدراسات : وتشمل الاختلافات بين أوقات الشفاء لدى نماذج الحيوان والتباين في نوعية العظم الموضعيةُ وكثافته للفحص النسيجي ولتقييم القياس الشكلي النسيجي (إلتصاق العظم وكتلة العظم) أوضح الفحص بالمجهر

الصوتي بأن استجابة العظم ، بصورة عامة، تجاه جميع العرسات كان متشابهاً جداً . ومن جانب آخر أفاد القياس الشكلي النسيجي للعظم بأن التصاق العظم إلى العرسة المخرشة والتي غُرزت بطريقة التحضير الأصغر حجماً لمكان العرسة كان أعلى بالمقارنة مع العرسات ذات السطوح المُحضرة آليا وفي استخدام الأساليب الجراحية الأخرى، إلا أن الفروق لم تكن هامة. لم توضح قياسات الكتل العظمية حدوث فروق واضحة بين فئات الدراسة و الأساليب الجراحية المطبقة . نستنتج من دراساتنا بأن طريقة التحضير الأصغر حجماً لمكان العرسة في العظم و ذات السطح المخرش يُعزز التصاق العرسة مع العظم.

ويحتوي **الفصل7** وصف لاستخدام عرسات بلمرية كانت تستخدم لتقييم استجابة العظم حول عرسة التيتانيوم بواسطة الرسم الطبقي بالحاسوب . كانت العرسات المستخدمة ذات مظهر لولبي حُضرت آليا وطُليت بطبقة من التيتانيوم بسماكة 400-500 نانو ميتر. غُرزت الغرسات في عظم الظنبوب و بعد 12 أسبوع أُخرجت من أمكنتها و تم تحضيرها للفحص بالرسم الطبقي بالحاسوب والمجهر الصوتي والتحليل المجهري بالأشعة السينية.
أظهرت الرسوم المحضَّرة بالأبعاد الثلاثة بشكل واضح بأن عظما قشرياً كان يحيط بالغرسات ولا يوجد أي نتاج صنعي مخطط . ووُجد بأن العظم كان نامياً داخل مسننات اللولب وكان يُرى متصلاً بحفرة نقي العظم و أوضح التقييم النسيجي بأن الغرسات المغطاة بالتيتانيوم كانت محتملة جيداً من قبل النسج وكان يُرى العظم في اتصال مباشر مع الطبقة المعطية للتيتانيوم. و إضافة إلى ذلك أظهر التحليل بالأشعة السينية وجود الكالسيوم و الفسفور التي تدل على وجود العظم . وقد أكد التحليل بالأشعة السينية البيانات الناتجة عن المجهر الصوتي .

وكنتيجة للتأثير الهام للطريقة الجراحية على ثبات الغرسة في العظم , جرى اختبار في الأحياء تم وصفه في **الفصل 5.** أستخدم في هذه الدراسة الميكانيكية 48عرسة بشكل البرغي و تم تحضير حشوية سطوحها آلياً أو بالتحريش (بالحمص) ووصعت داخل لقمة عظم العحد للماعز. حُضرت أماكن الغرس إما بالطريقة التقليدية أو بالتحضير الأصغر حجماً لمكان الغرسة.

جرى تقييم قوة الوجيهة (سطح الإلتصاق) ومظهر العظم بعد 12 أسبوع من الغرس باستخدام اختبار عزم التدوير و المجهر الالكتروني التفرسي. كانت قيمة تدوير إخراج الغرسات المحرشة المعروزة بطريقة التحضير الأصغر حجماً لمكان الغرسة (29 ± 98) وكانت ذات معنوية إحصائية أعلى بالمقارنة مع الغرسات التي تم تحضير سطحها بالآلة ووصعت بطريقة قطع العظم بالأزاميل الخاصة. أوضح المجهر الالكتروني التفرسي بأن جميع الغرسات أظهرت التصاقاً مع العظم . بالإضافة إلى ذلك فقد نتج عن اختبار عزم التدوير في جميع الحالات التجريبية كسراً في طبقة الوجيهة بين الغرسة والعظم . وعلى ذلك فإننا نستنتج بأن وضع الغرسات المخرشة باستخدام طريقة التحضير الأصغر حجماً لمكان الغرسة يؤدي إلى قوة ارتباط عالية لها مع نسج العظم المحيطة.

وبعد ذلك يعرض **الفصل 6** وصفاً لنتائج التحليل النسيجي لتأثير السطح الطبغرافي للغرسة والطريقة الجراحية على استجابة العظم. أستخدم في هذه التجربة 48 عرسة بشكل البرغي خُضرت سطوحها آلياً أو بالتخريش . غُرزت الغرسات في الجانب الأيسي الأيسر و الأيمن للقمة عظم العحد لدى 8 حيوانات من الماعر باستخدام ثلاث طرق جراحية مختلفة : طريقة الصغط المطابق (قطر الغرسة يساوي قطر مكان الغرسة) وطريقة التحضير الأصغر حجماً لمكان الغرسة (قطر مكان الغرسة أصغر من قطر الغرسة) وطريقة قطع العظم بالأزاميل الخاصة.

وضع في كل لقمة عظم 3 غرسات , وبعد 12 أسبوع من فترة الغرس أُخرجت الغرسات من أمكنتها وتم تحضيرها

يستنتج من هذه التجربة بأن للطريقة الجراحية المطبقة تأثير حاسم على ثبات الغرسة في العظم.

وفي **الفصل 4** يوجد وصف للمراجعة المنتظمة التي جرت لتقدير نسبة ديمومة الغرسات التي وُضعت بطريقة قطع العظم. جرى البحث عن المطبوعات المنشورة بين 1953 -2005 باستخدام قاعدة البيانات ميد لاين ووُجد 164دراسة . كانت معايير تضمين الدراسات المقبولة هي الدراسات السريرية أو التقارير السريرية حول استقصاء طريقة قطع العظم.لوضع الغرسات السنية والفئات الشاهدة أوفئات الإختبار من الدراسة السريرية أو التقرير السريري حتى لو أن فئة (أو فئات) أخرى لم تتطابق مع معايير أخرى . تم اختيار13 مقالة في المرحلة الأولى من البحث واستبعدت 151 مقالة. كانت معايير قبول الدراسات هي الدراسات السريرية أو التقارير السريرية التي تستخدم طريقة قطع العظم مع الغرسات السنية و طريقة قطع العظم التي تستخدم في تحضير مكان الغرس مع أو بدون رفع قعر الجيب. و في المرحلة الثانية تم اختيار خمسة مقالات تؤمن معايير تضمين الدراسات.

وبمُعالجة بيانات الدراسات التي تم اختيارها, كانت منحنيات الديمومة الإجمالية للغرسات قد رسمت للفترات قبل و بعد التحميل. أظهرت البيانات المشتركة لـ 349 عرسة احتمالات ديمومة بنسبة 98%(97.2%-100) حتى وقت التحميل و(94%-100%) 99 بعد 56 شهر من التحميل. وفي نهاية فترة المراقبة كانت 41عرسة (18مريض) مازالت معرضة للخطر.

نستنتج من هذه المراجعة أن بيانات إبدار الغرسات الموضوعة بطريقة قطع العظم (بالأزاميل الخاصة) تبدو مشابهة للبيانات المتعلقة بالغرسات التي وضعت بطريقة الثقب التقليدية .

جميع الدراسات تقريبا تزايدا في اتصال العظم مع الغرسة كلما زادت حشوية سطح الغرسة . ووجدت أيضاً علاقة هامة بين قوة إخراج الغرسة من مكانها وحشوية السطح. ولسوء الحظ كانت الدراسات النهائية التي تم اختيارها غير متجانسة بشكل كبير من أجل استنباط البيانات, و استنادا إلى الدراسات الأولية, أستنتج بأن البيانات المتوافرة قدمت بيانات داعمة للعلاقة الايجابية بين اتصال العظم مع الغرسة وحشوية سطح الغرسة.

وجرى فيما بعد دراسة تجريبية في المخبر كما هو موصوف في **الفصل 3** لاستقصاء تأثيرات سطح الغرسة والطريقة الجراحية المطبقة على ثبات الغرسة. ومن أجل ذلك أختيرت غرسات بشكل البرغي تم تحضير حشوية سطوحها بالآلة أو بالتخريش بالحمض ووضعت في لقمة عظم فخذ الماعز.

جرى تحضير أمكنة الغرسات إما بالطريقة التقليدية. (الثقب) أو بالتحضيرالأصغر حجماً.(ثقب العظم بحيث يكون حجم مكان الغرسة أصغر من حجم الغرسة) أو بطريقة قطع العظم.(بالأزاميل الخاصة). جرى تحديد عزم تدوير الغرسة أثناء غرزها وإخراجها واتصالها مع العظم و المظهرالتشكلي للعظم بواسطة المجهر الالكتروني التفرسي (المقطعي).والفحص الطبقي المحوسب
لقد وجدنا بأن قيم عزم التدوير في.غرز وإخراج الغرسة كانت ذات أهمية إحصائية أعلى في الغرسة المخرشة التي أُدخلت بطريقة التحضيرالأصغر حجماً لمكان الغرسة (115.2+/- 31.1, 102.9 +/-36.4نيوتن سم) بالترتيب. إضافة إلى ذلك كان معدل قيم اتصال العظم مع الغرسة أعلى في الغرسات المخرشة والموضوعة بطريقة التحضيرالأصغر حجما لمكان الغرسة (87.5 +/-5.6) , و كان ذو معنوية إحصائية بالمقارنة مع الغرسات المحضرة بالآلة أو بالتخريش بالحمض والتي غُرزت بالتقنية التقليدية .

ملخص. استنتاجات عامة ونظرات مستقبلية

لم تقدم البيانات التجريبية المتوافرة حتى الآن جواباً واضحاً ونهائياً حول أهمية الطريقة الجراحية المطبقة في غرس الأسنان. كان الهدف من الدراسات المقدمة في هذه الأطروحة هو استقصاء تأثير الطريقة المستخدمة في وضع الغرسة والعلاقة بخشونة سطحها، على التثبيت العظمي النهائي لها. ومن أجل هذا الغرض طرحت الأسئلة التالية :

1- هل يؤدي سطح الغرسة الأكثر خشونة إلى اتصال أكبر للعظم مع الغرسة ؟

2- هل يؤدي سطح الغرسة الأكثر خشونة إلى مقاومة أكبر لعزم تدوير الغرسة ؟

3- هل تعد الطريقة الجراحية المطبقة واحدة من المعالم الرئيسية للسلوك النهائي للعظم مع الغرسة والتي ربما تكون أكثر أهمية من معايير سطح الغرسة مثل الخشونة و التركيب ؟

4- هل يمكن لطريقة جراحية خاصة أن تزيد من نسبة ديمومة الغرسات ؟

5- ما هي تأثيرات الطرق الجراحية المستخدمة على الثبات النهائي للغرسة وعلى حالة العظم ؟

ملخص

للنظر بعمق في البيانات المتوافرة حالياً حول خشونة سطح الغرسة، يعرض **الفصل2** مراجعة منتظمة للدراسات الاستقصائية التي جرت حول تأثيرات خشونة سطح الغرسة على استجابة العظم وعلى تثبيت الغرسة.

أظهر البحث في قاعدة البيانات ميدلاين وجود أكثر من 5900 ملخص حول أبحاث غرس الأسنان، وبعد تطبيق معيار استبعاد / تضمين الدراسات ، تم اختيار 470 مقالة في المرحلة الأولى من البحث ثم 23 مقالة في المرحلة الثانية ثم 14 مقالة في المرحلة الثالثة والنهائية.

و بسبب وجود الاختلاف الواسع في البيانات المتعلقة بالمطبوعات المنشورة الحالية، فقد منع ذلك من إجراء تحليل تجميعي لها و استبدل بالمراجعة المنتظمة. أظهرت

ملخص البحث

شكر

بعد مضي ست سنوات ونصف من الغربة, منها ثلاث سنوات ونصف قضيتها لانجاز هذا البحث, اجدها فرصة للتقدم بالشكر لكل من ساعدني في اول خطوات رحلتي العلمية وخلال فترة دراستي وحتى انتهائي.

اشكر وزارة الصحة التي منحتني هذه الفرصة للدراسة.

ابعث شكري وتقديري للاب الدكتور اسامة شبكشي. دكتور اسامة كلماتك لي, كانت دافع قوي لاتمام هذا العمل.

اتقدم بالشكر للملحق التعليمي بالمانيا.

واخيرا اشكر والداي لدعمهم لي. لم ولن انسى ما فعلتماه من اجلي.

اشكر زوجي وابنائي لوقوفهم بجانبي وغفران انشغالي عنهم.

اهداء الى:

والداي

زوجي

ابنائي

تأثير الطرق الجراحية المطبقة في غرس الأسنان على التثبيت العظمي للغرسة

منال معتوق شلبي